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STUDIES ON THE EFFECT OF OCULAR HYPERTENSION UPON THE CHRONAXIA OF THE HUMAN OPTIC SYSTEM

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I. Studies on the Chronaxia of the Normal Human Optic System

Systemic studies on the electric physiology of the human optic system were made by DuBois-Raymond, Weiss-Hoorweg and also in Japan by Kuwabara, Motegi, Imaizumi, Yonemura and Narasaki etc.. The experiments made by these authors were under the conditions of dark adaptation of the eyes.

Up to now, except for the clinical examinations for glaucomatous eyes, the full reports of studies on the effect of ocular hypertension upon the chronaxia of the human optic system, are not yet at hand.

In this communication that pretends to be but a preliminary report the chronaxia of ten normal human eyes was tested and statistical studies were also made.

Experimental Methods

In accordance with Bourguignon's original method, the authors measured the chronaxia of human eyes, with a chronaximeter, under the discharge of condensers.

As subjects ten adult eyes of normal visual acuities were selected.

The experiments were made under the same conditions. Constant illumination of the examination room and body conditions of subjects were carefully considered. Under these conditions both rheobase and chronaxia were measured by direct and indirect methods as described by Bourguignon.

Results and Comment

1) The rheobase and chronaxia of ten normal human eyes were measured, the mean values of which were as follows:

Direct rheobase (D.R.) 7.04 Volt (v.)
Indirect rheobase (I.R.) 7.04 Volt (v.)
Direct chronaxia (D.C.) 0.692 μF.
Indirect chronaxia (I.C.) 0.655 μF.

Up to now, several studies on the chronaxia of the human optic system were reported by Bourguignon, Déjean, Achilles, Merkulow, Pollard, Kreindler, Becher, Motegi and Matsuyama etc..

According to the data studied by Motegi, D.R., I.R., D.C. and I.C. are 5.5V., 5.2V., 0.498 μF. and 0.375 μF. respectively. Matsuyama describes these values as 5.9V., 5.7V., 0.434 μF. and 0.433 μF. respectively.

As compared with these values the slight increase of rheobase and lengthening of chronaxia were observed in our experiments.

2) Reciprocal interrelation between the chronaxia and rheobase

By measuring both chronaxia and rheobase of ten normal eyes the authors obsered the reciprocal interrelation of I.R. and D.R., I.C. and D.C., I.R. and I.C., D.R. and D.C. in the same individual with a statistical significance (standard error below 1%).

This indicates, that the four values have always interrelative variations in normal eyes and therefore it is suggested that there are pathological findings in the reception system (rod or cone) when the isochronism of each value cannot be observed.

3) Diurnal and individual variations of rheobase and chronaxia

Rheobase and chronaxia of ten normal eyes were measured.

Each eye was examined five times at intervals of five to ten days. According to the statistics the I.C. showed a significance of differences, while all differences of other values were considered to be not worth deliberation because they were regarded as experimental errors.

4) The effect of an experimental process of one eye upon the chronaxia of other eye, when the chronaxia of both eyes were measured continuously (Table 1)

Table 1. Relation between the Chronaxie of one Eye and that of another Eye when measured consecutively

	R-Eye				L-Eye Immediately after				L-Eye After an hour			
	Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)	
	I.C.	D.C	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.
No. 1	12	14	0.380	0.464	13	10	0.326	0.435	11	12	0.378	0.474
No. 2	7	7	0.435	0.539	6	6	0.632	0.620	7	7	0.598	0.621
No. 3	5	8	0.501	0.300	5	8	0.398	0.360	5	8	0.406	0.382
No. 4	3	3	0.487	0.670	4	4	0.440	0.690	4	4	0.532	0.721
No. 5	4	6	0.690	0.755	6	8	0.622	0.490	5	7	0.701	0.585
No. 6	7	6	0.399	0.889	6	8	0.379	0.369	7	7	0.349	0.326
No. 7	7	8	0.587	0.688	5	6	0.699	0.737	5	6	0.734	0.755
No. 8	9	8	0.399	0.568	13	13	0.469	0.395	12	12	0.460	0.425
No. 9	9	10	0.642	0.651	9	10	0.671	0.720	9	9	0.677	0.728
No. 10	8	8	0.730	0.821	7	8	0.721	0.720	8	7	.0711	0.716
								(%)	α>50	α>50	30>α >20	30>α 20>

Both, the rheobase, and chronaxia of one eye were examined immediately and one hour after the same experimental treatment of other eyes. Statistical significance

between the two values could not be observed under the standard errors of 5 %. This indicates, that the experimental process of one eye did not exercise any influence upon the chronaxia of other eye. From this fact the authors considered that the electric excitability of the optic system might be caused not by a stimulation conducting element, but by a centripetal neuron previously reported.

5) Chronaxia influenced by the time element. (Measured after 10, 30 and 60 minutes) Table 2. and 3.)

Table 2. Chronaxie influenced by the Time Element (measured after 10 minutes and an hour)

	R-Eye				R-Eye After 10 minutes				R-Eye After. 1 hour and 10 min.			
	Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)	
	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.
No. 1	7	6	0.278	0.300	9	10	0.360	0.632	7	6	0.280	0.384
No. 2	6	7	0.654	0.749	10	4	1.025	1.049	6	7	0.650	0.645
No. 3	5	6	0.549	0.480	4	6	0.730	0.320	5	7	0.540	0.632
No. 4	7	9	1.000	0.657	5	7	0.962	0.469	7	9	0.940	0.702
No. 5	5	7	0.996	0.520	8	7	0.720	0.520	4	6	1.032	0.605
No. 6	7	10	0.790	0.689	7	12	0.631	0.532	7	8	0.620	0.900
No. 7	7	8	0.390	0.718	8	9	0.608	0.814	7	8	0.491	0.534
No. 8	9	8	0.989	0.613	5	8	0.719	0.531	8	8	0.801	0.724
No. 9	9	10	0.668	0.492	13	15	0.714	0.531	7	9	0.703	0.718
No. 10	6	7	0.765	0.820	10	10	0.823	0.916	6	8	0.672	0.812
				α(%)	$10>\alpha>5$	$30>\alpha>20$	$\alpha>50$	$\alpha>50$	$\alpha>50$	$30>\alpha>20$	$30>\alpha>20$	$20>\alpha>10$

In order to examine the influence of the time element upon the chronaxia of the same eye, when it is measured consecutively, the authors compared the chronaxia with that measured 10, 30 and 60 minutes after the first experimental treatment.

Only in I.C. measured after 30 minutes the statistical significance of its differences was observed, while in all other cases the influence of the experimental process at the first time upon chronaximetry remained out of the question.

II. The Influences of Bulbar Compression Upon the Chronaria of the Human Optic System

In this communication the authors examined the influences of bulbar compression upon the chronaxia of the normal human optic system. The chronaxia of ten normal human eyes were measured under the compression of the eye bulbus with a Bailliart's

ophthalmodynamometer (100gr., 70gr., 50gr.). The duration of this bulbar compression was 10 minutes respectively. The experimental method was the same as reported in part I. Statistical studies were also made.

Results

1) Immediately after the bulbar compression of 50gr. the I.R. of nine eyes were increased, while that of one eye was decreased. The mean value of the increase was 2.4 V..

2) The influences of the bulbar compression of 70gr. upon the chronaxia and rheobase.

Immediately after the bulbar compression. The increase of I.R. in eight eyes, the decrease of I.R. in one eye were observed, while one eye was unchangeable. The mean value of the increase was 1.1 V..

The increase of D.R. in 7 eyes, the decrease of D.R. in one eye; unchangeable in 2 eyes. The mean value of the increase was 2.6 V..

The lengthening of I.C. in 7 eyes; the shortening of that in 3 eyes; the mean value of the lengthening, 0.305 μF.. The lengthening of D.C. in 9 eyes; the shortening of that in one eye; unchangeable in one eye. The mean value of the lengthening 0.445 μF..

Table 3. Chronaxie influenced by the Time Element (measured after half an hour and one hour and a half)

	R-Eye				R-Eye After half an hour				R-Eye After 1 hour and half			
	Rbeobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)	
	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.
No. 1	8	8	0.476	0.512	10	8	0.482	0.551	8	7	0.442	0.501
No. 2	7	7	0.765	0.839	10	6	0.731	0.831	7	8	0.781	0.805
No. 3	6	6	0.739	0.690	7	7	0.741	0.632	6	6	0.581	0.490
No. 4	5	5	0.800	0.659	5	6	0.829	0.610	6	5	0.879	0.663
No. 5	5	7	0.540	0.649	9	7	0.529	0.601	5	7	0.580	0.528
No. 6	7	6	0.549	0.419	6	10	0.525	0.401	7	6	0.565	0.406
No. 7	8	8	0.495	0.532	9	8	0.432	0.549	9	8	0.429	0.490
No. 8	8	8	0.490	0.430	8	7	0.432	0.349	9	8	0.492	0.438
No. 9	9	9	0.729	0.729	7	6	0.727	0.743	8	7	0.706	0.728
No. 10	7	8	0.720	0.730	4	8	0.735	0.759	6	8	0.747	0.772
				α(%)	5>α>2 *	α>50	20>α>10	30>α>20	α>50	30>α>20	α>50	20>α>10

Table 4. Influence of the Bulbar Pressure (50gr.) upon the Chronaxie of Normal Optic System

	Before the Pressure				Immediately After				After Half an hour				After an hour			
	Rheobase (V.)		Chronaxia (μ.F.)		Rheobase (V.)		Chronaxia (μ.F.)		Rheobase (V.)		Chronaxia (μ.F.)		Rheobase (V.)		Chronaxia (μ.F.)	
	I.C.	D.C.	I.C.	D.C.	I.C.	D.C	I.C.	D.C.	I.C.	D.C	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.
No. 1	6	11	0.578	0.909	11	11	0.562	0.399	14	11	0.580	0.960	12	11	0.488	0.889
No. 2	7	7	0.654	0.605	11	10	0.932	0.932	8	8	0.870	0.768	8	7	0.780	0.568
No. 3	8	9	0.549	0.708	9	8	0.800	0.499	7	8	0.898	0.589	8	8	0.836	0.750
No. 4	4	8	1.000	0.990	6	6	0.958	0.901	5	6	0.730	0.858	4	5	1.000	0.796
No. 5	5	7	0.996	0.492	6	5	0.500	0.400	7	8	0.831	0.533	7	8	0.768	0.399
No. 6	7	11	0.790	0.500	9	10	0.559	0.500	6	11	0.678	0.769	7	11	0.500	0.308
No. 7	8	13	0.396	0.389	7	9	0.656	0.576	8	8	0.477	0.888	6	13	0.377	0.498
No. 8	8	8	0.989	1.205	10	8	2.848	3.985	11	13	0.525	1.768	10	10	2.889	1.997
No. 9	9	16	0.668	0.428	14	19	0.598	0.490	10	11	0.459	0.488	9	11	0.599	0.413
No. 10	6	7	0.765	0.893	9	9	0.790	1.201	10	10	0.632	0.895	8	7	0.454	0.887
				α (%)	1>α *	50>α >40	40>α >30	40>α >30	10>α >5	α>50	30>α >20	20>α >10	20>α >10	40>α >30	α>50	α>50

30 minutes after the bulbar compression. The increase of I.R. in 5 eyes ; the decrease of that in one eye ; unchangeable in 4 eyes. The mean value of the increase, 2.3 V..

3) The influences after the bulbar compression of 100gr..

Immediately after the bulbar compression. The increase of I.R. in 7 eyes ; the decrease of that in 2 eyes ; unchangeable in one eye. The mean value of the increase, 1.9 V.. The lengthening of D.C. in 7 eyes ; shortening of that in 2 eyes ; unchangeable in one eye. The mean value of lengthening, 0.231 μF.

30minutes after the bulbar compression. The increase of I.C. in 8 eyes ; the decrease in one eye ; unchangeable in one eye. The mean value of the increase, 1.9 V..

Generally speaking, after the bulbar compression the rheobase in many cases was influenced and the lengthening of chronaxia in all cases was observed.

From these experimental results the authors could come to the following considerations.

a) Both rheobase and chronaxia are more markedly influenced by the bulbar compression of 70gr. and 100gr. than that of 50gr..

b) The rheobase are more strongly influenced by the bulbar compression than the chronaxia.

c) The indirect phosphone reaction is stronger than the direct phosphone reaction.

Table 5. Influence of the Bulbar Pressure (70gr.) upon the chronaxie of Normal Human Optic System

	Before the Pressure				Immediately After				After half an hour				After an hour			
	Rheobase (V.)		Chronaxie (μ.F).		Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)	
	I.C.	D.C.	I.C.	D.C	I.C.	D.C.	I.C.	D.C	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.
No. 1	8	9	0.539	0.499	10	10	0.688	0.645	11	7	0.519	0.498	8	8	0.660	0.567
No. 2	5	5	0.938	0.769	6	6	0.889	0.787	5	5	0.789	0.787	6	6	1.007	0.767
No. 3	7	5	0.499	0.982	5	4	1.384	1.770	7	5	0.509	0.937	6	5	0.325	0.900
No. 4	7	6	0.494	0.496	8	9	0.794	0.933	7	7	0.868	0.498	7	8	0.786	0.499
No. 5	6	6	0.500	0.971	6	7	0.580	1.697	6	12	0.995	0.465	6	7	0.490	0.987
No. 6	5	10	0.598	0.598	7	18	0.477	0.788	8	13	0.477	0.799	7	14	0.477	0.598
No. 7	9	13	0.346	1.867	10	22	0.980	1.667	18	22	0.456	2.077	15	15	0.386	1.650
No. 8	8	8	0.842	0.982	10	8	1.950	2.324	10	8	1.525	0.824	6	10	1.000	0.800
No. 9	7	9	0.498	0.500	10	13	0.658	0.500	11	15	0.346	0.396	11	6	0.398	0.480
No. 10	8	8	0.820	0.793	9	8	0.728	0.901	8	8	0.890	0.803	6	11	0.816	0.811
				α(%)	5>α>2*	5>α>2*	5>α>2*	5>α>2*	5>α>2*	10>α>5	20>α>10*	40>α>30	20>α>10	α>50	30>α>20	α>50

Comment

The pressure of the retinal central artery corresponds to 50-60 mmHg., 70-75 mmHg. and 90-102 mmHg. respectively when it is measured under the bulbar compression of 50gr., 70gr. and 100gr. with a Bailliart's ophthalmodynamometer under the condition of ocular tension with 15-25 mmHg..

Therefore it is thought, that under the bulbar compression of 50gr., there may be a congestion of the ocular vascular system and under the compression of 70gr. which exceeds the normal pressure of the retinal central artery the vascular system of the eye will become more markedly congestive, and the bulbar pressure of 100gr. will stop the blood circulation of the ocular vessels.

Cibis, Suda and Koyama observed the enlargements of blind spots under the bulbar compression which exceeded the minimal pressure of the retinal central artery and they considered, that this phenomenon might be caused by retinal edema after the circulatory disturbances of retinal blood vessels.

Studying on the influence of atmospheric depression upon the ocular tissues, Imaizumi observed in his experiments a ring shaped scotoma and he thought that it was caused by the defficiency of oxygen.

Histological examinations of the ocular tissues, after the bulbar compression were made by Wegner, Guist and Amano. Especially Amano observed the degenerations in

Table 6. Influence of the Bulbar Pressure (100gr.) upon the Chronaxie of Normal Human Optic System

	Before the Pressure				Immediately After				After half an hour				After an hour			
	Rheobese (V.)		Chronaxie (μ.F.)		Rneobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F.)		Rheobase (V.)		Chronaxie (μ.F)	
	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C.	I.C.	D.C	I.C.	D.C.
No. 1	10	13	0.500	0.898	13	10	0.982	0.468	9	11	0.465	0.730	10	10	0.448	0.774
No. 2	7	9	0.499	0.530	9	14	0.578	0.598	10	10	0.490	0.530	10	10	0.408	0.500
No. 3	3	6	0.627	0.547	4	4	0.596	0.500	6	6	0.499	0.499	5	6	0.499	0.499
No. 4	7	8	0.777	0.480	6	8	0.798	0.480	5	5	1.000	0.556	7	6	0.890	0.595
No. 5	5	5	0.490	0.488	5	7	0.869	0.990	5	7	0.927	0.758	5	5	0.560	0.490
No. 6	7	8	0.625	0.512	9	8	0.722	0.544	9	8	0.550	0.550	7	8	0.756	0.532
No. 7	11	12	0.692	0.378	16	14	0.624	0.728	9	16	0.499	0.483	10	12	0.577	0.498
No. 8	7	8	0.972	0.996	10	10	1.201	1.303	11	10	1.050	1.703	8	8	0.100	1.200
No. 9	10	10	0.996	0.856	14	15	1.868	1.898	13	15	0.766	0.780	11	10	0.750	0.764
No. 10	8	7	0.390	0.498	8	8	0.498	0.498	9	8	0.399	0.480	8	8	0.383	0.498
				α(%)	2>α >1 *	30>α >20	α>50	10>α >5	1>α	30>α >20	α>50	40>α >30	α>50	α>50	α>50	30>α >20

the ganglion cell layer of the retina after the bulbar compression which exceeded the pressure of the retinal central artery.

According to Bourguignon the indirect and direct phosphone reactions of the optic system are caused by the ganglion cells and the bipolarcells of the retina respectively, so that the bulbar compression does influence mainly the ganglion cell layers.

Therefore, as a conclusion, it is considered, that the changes of rheobase and chronaxia after the bulbar compression mignt be caused not by the influence of ocular hypertension but by the changes of electric excitability of the optic system after the circulatory disturbances of the ocular tissues.

(Published in Acta Ophth. Jap. 63:3964, 3972, and 4419, 1959 in Japanese.)

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THE HISTOLOGICAL INVESTIGATION ON THE NERVES OF THE EXTRINSIC OCULAR MUSCLES OF THE RABBIT

Sumio OMOTO

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In this experiment the author made histological investigation on the following subjects:

1) The calculation and fibre-analysis of the third nerve, fourth nerve, and sixth nerve of the rabbit.

2) The afferent fibres from the extra ocular muscle receptor of the rabbit.

3) The innervat ratio for the superior oblique muscle of the rabbit.

4) The ganglion cells along the roots of the sixth nerve of the rabbit and the course of the cranial sympathetic nerve.

These problems have been studied by serveral authors, but there is still disagreement especially as to the afferent fibres or the nature of the ganglion cells.

Material and Method

Rabbits were used throughout this investigation. The 3rd, 4th, 6th nerve was completely removed from its exit to the entrance of its innervationg muscles with the ophthalmic nerve originated from the Gasserian ganglion.

These nerves were removed with great care to avoid crushing the anatomical and mutual relation or stretching the nerve fibres at the cavernous sinus or in the orbit. The normal saline solution was used to prevent drying.

These nerves were put into 1% osmic acid for 24-48 hours, embedded in hard paraffin and serial sections 5μ thick were cut.

Small nerve fibres were suitable for osmic acid stain.

The parts of these nerves in another case were stained by the silver impregnation (of Bielshowsky) method.

The count and measurement of the nerve fibres were made with aid of the microscopic-photograph under higher magnification (400x). The superior oblique muscle was dealt with in a same way.

In addition the degenerations experiment, cutting through the ophthalmic division of the fifth nerve, was made to trace the course of the afferent fibres.

Results and Discussion

On the calculation and fibre-analysis of the extra ocular nerve (Table 1)

The parts to have been counted were shown by simplified diagram in Fig 1.

The 3rd nerve: it contained 4827 myelinated fibres at the exit from the brain and the diameter of these nerve fibres ranged from 1μ to 15μ with two peaks at 2-3 μ and 5-7μ. (as shown in Fig 2).

Table 1. Fiber-Analysis of N III, N IV, & N VI of the rabbit

N / Cal	N III					N IV				N VI			
	R.Sup	R.inf	total	Trunk	vary	T_1	T_2	T_3	T_1/T_3	A_1	A_2	A_3	A_1/A_3
thick over 6μ	61 (4,4)	237 (6,3)	298 (5,9)	905 (18,7)	− 617	437 (50,4)	419 (45,2)	44 (4,9)	− 18	554 (38,4)	281 (18,8)	126 (8,8)	− 428
medium 3~6 μ	856 (61,8)	2118 (59,5)	2874 (59,8)	2439 (50,5)	+ 490	192 (21,9)	224 (24,2)	584 (65,8)	+ 34	533 (37,8)	846 (57,0)	886 (58.4)	+ 351
fine under 3μ	472 (33,9)	1240 (34,2)	1712 (34,3)	1484 (30,8)	+ 183	238 (27,7)	282 (30,6)	258 (29,3)	+ 44	326 (23,8)	360 (24,2)	504 (33,3)	+ 178
% to the total number	1389 (100,0)	3595 (100,0)	4984 (100,0)	4828 (100,0)	+ 156/3,2 %	867 (100,0)	927 (100,0)	886 (100,0)	+ 60/6,9 %	1413 (100,0)	1487 (100,0)	1514 (100,0)	+ 101/7,1 %
Part	A	B		C		D	E	F		G	H	I	

Fig. 1. Diagram to show the innervation of the extrinsic eye muscles of rabbits.

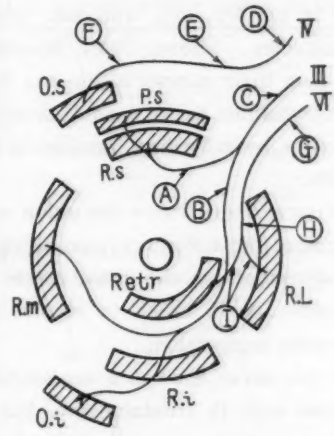
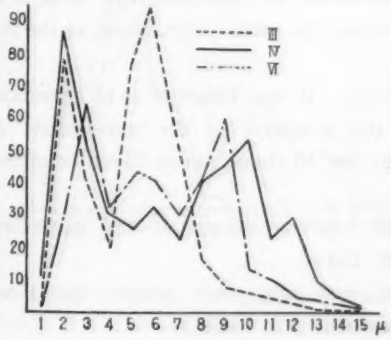


Fig. 2. Fiber-Analysis of N III, N IV, & N VI of the rabbit at the exit from the brain.



Thick fibres decreased from 18.3% to 5.9% on their course distalwards, conversely medium sized fibers and fine fibres increased each by 8.3% and 3.5%.

The incnease of nerve fibres distalwards in the nerve-trunk (distal excess) was recognized by 3.2%, and nerve fibres taking part in this distal excess were thick fibres which were bifurcated and dichotmized towards their destination.

It must be obvious that the parasympathetic fibres, which arrive at the ciliary ganglion, are found in the R. inf. or trunks of the 3rd nerve.

Fine nerve fibres groups, which consisted of 5-30 nerve fibres 1-5μ in diameter, were noted scattered in the nerve-trunk, perhaps they seemed to be belonging to the parasympathetic, but one can not differentiate these nerve fibres groups from motoric or sensory or extrapyramidal nerve fibres which were accepted to be found in the eye muscle in results of the investigation on the nerve endings.

The 4th nerve: it contained 867 myelinated fibres, the size of these

nerve fibres ranged from 1-15μ with two peaks at 2-3μ and 8-10μ in the proximal part and at 2-3μ and 4-5μ in the distal part.

The distal excess was recognised by 6.9% at the 6mm distal.

The 6th nerve: this nerve-composition was almost the same as the above mentioned two nerves, ranging from 1-15μ with two peaks at 2-3μ and 8-9μ

The increased fibres in the distal excess, as Sasaoka (1934) pointed out, were medium sized fibres not fine fibres.

The afferent fibres from the extra ocular muscle receptor of the rabbit

In this investigation by means of serial section, the communications between the frontal nerve and trochlear nerve were noted in the orbit and in the cavernous sinus. (as shown in Fig19~26), but the communication connecting the sixth nerve or third nerve with the ophthalmic division were noted neither in the cavernous sinus nor in the orbit.

Although afferent fibres are known to be present in the 3rd, 4th, and 6th nerve, their points of entrance into these nerves are still unknown. Stibbe (1926), Winchler (1932), Kiss (1935) presumed that the afferent fibres took their course within the fifth nerve on the base of the communication with the ophthalmic nerve, and Whitteridg (1949) also obtained physiological evidence for this course by recording impulses in the nerve from the inferior oblique of goats during stretch.

In this case the Trochlear contained 835 myelinated nerve fibers before the union with the frontal nerve and 866 myelinated fibres after the union, the difference amounting to 6.1%, but it was obscure, whether this increase depended on the distal excess or mixture of the sensory fibres sent form the frontal nerve, so in order to resolve the cause of this increase, the degeneration experiments were undertaken.

After the severance of the ophthalmic nerve, the 4th nerve showed a considerable number of degenerated fibres distalwards to the union with th frontal nerve, but in the histological investigation just distal to the Gasserian ganglion it was made clear, that the 4 th nerve was already severed with the ophthalmic nerve in the course of the operation, as Sherrington (1903) stated on the same accident.

From the results above mentioned, receptor fibres of the extrinsic eye muscle of rabbits seemed to run throughout their course within the motor nerve such as the 3rd, 4th, and 6th nerve.

The innervate ratio for the superior oblique muscles It was believed to be correlated between the number of the nerve fibres and the precision of the movement. As Adler (1953) stated, eye muscles were supplied by the 10 times nerve fibres compared with the ordinary skeletal muscles.

In the observation, the innervate ratio for the superior oblique of the rabbit was 5.6, that is, 886 nerve fibres supplying 4997 muscle fibres.

The values of the eye muscles in the dog, cat, and frog were around the same.

The data quoted from the previous work were shown in table 4.

The diameter of the muscle fibres of the superior oblique ranged from 2.5 to 36μ with a peak at 18μ, (as shown in Fig 3) and there were no correlations between the distribution of muscle fibres and of their innervating nerve fibres.

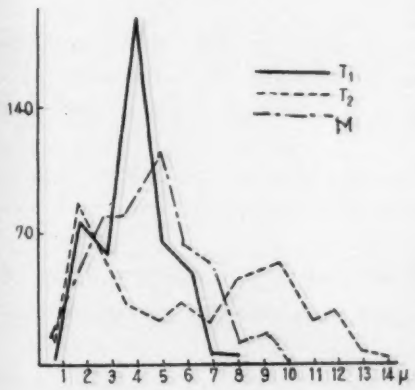
On the ganglion cells along the roots of the sixth nerve and the course of the cranial sympathetic nerve.

Tomsen (188) was the first to recognise the ganglion cells on the trunke of the ocular nerve. Since then several authors noted these ganglion cells in some kinds of animals. The nature of these ganglion cells is not yet ascertained, that is, there are different opinions to regard them as a group of migrated posterior-root cells, or group of the ciliary ganglion cells or sympathetic ganglion cells or those related to the proprioceptic. But their number were not sufficient to supply all the proprioceptive fibres of the eye muscle.

Table 2. Number of the Ocular Nerve Fibers of the Rabbts (Silber Stain)

	Prox
Nerv Ⅲ	5471
N. Ⅳ	875
N. Ⅵ	1473

Fig. 3. Fibre-Analysis of the 4th nerve and of the Superior oblique muscle.
T_1·····Distal part
T_2·····Proximal Part
M·····muscle fibre



(nerve fibre)
6 9 12 15 18 21 24 27 30 33 36μ (muscle fibre)

In this investigation, the ganglion cells along the roots of the sixth nerve in the cavernous sinus, which ares sufficiently numerous to constitute defininte ganglia, seemed to have communication with the pterigopalatine ganglion and receive fibres from the ophthalmic nerve and sympathetic nerve, so the nature of the ganglion cells appeared to be parasympathetic (as shown Fig 30~33)

In the same experiment cranial sympathetic nerves were noted to run into the perineulium of the 6th nerve medial to the Gasserian ganglion and left in the cavernous sinus to compose the plexsus. (Fig 34)

The sympathetic nerves, as Raeder (1924) described, were not found in the nasociliary nerve, but rather running down along the nerve.

Summary

1. The 3rd, 4th and 6th nerve fibres amount to 4827, 867, 1413 at the exit from the brain.

2. Each nerve trunk contains in the distal part more fibres than in the

Table 3. Number of the Extra Ocular Nerve Fibres

N	Human		Dog	Cat	Rabbit
	Vierordt	Toyota	Takahasi	Tatesi	Takahasi
Nerv III	15000	18802	11428	Prox R. sup 1971 9468 R. inf 7875	(A) 6597 (B) 5441
Nerv IV	2147	2256	1369	1120	757
Nerv VI	3500	4821	2227	1961	1675

Table 4. Innervat Ratio

Human's eye muscle (Tergert, Bors)	Sheep's eye muscle (Tergert)	Rat's eye muscle (Ibayasi)	Frog's eye muscle (Tergert)	Frog's hand. m. (Tergert)	Cat's Laryngial m. (Od ate)	Human's Soleus m. (Bors)	Rabbit's eye muscle (Omots)
1:2,3 1:4,3—5.9	1:5,5	1:6	1:3—4	1:30	1:30	1:47,5	1:5,6

proximal part, the difference amounting to 5% approximately.

3. Each distributive curve was exhibited in two maximal groups.

4. The communications between the frontal nerve and trochlear nerve were noted in the orbit and in the cavernous sinus.

5. The trochlear nerve fibers amount to 835 before the union with the frontal nerve and 886 after the union, the difference amounting 6.1%, but it was obscure, whether this increase depend on the distal excess or mixtur of the sensory fibres sent from the frontal nerve.

6. The communications connecting the sixth nerve or third nerve with the ophthalmic division were noted neither in the cavernous sinus nor in the orbit.

7. The innervat ratio for the superior oblique of the rabbit was 5.6, that is, 886 nerve supplying 4997 muscle fibers.

The values of the eye muscles in the dog, cat, and frog were around the same.

8. The diameter of muscle fibres of the superior oblique ranged from 2,5 to 46μ, with a peak at 18μ

9. The ganglion cells along the roots of the sixth nerve seemed to have communications with the pterygopalatine ganglion and receive fibres from the ophthalmic nerve and sympathetic nerve.

10. The cranial sympathetic nerves run into the perineulium of the sixth nerve medial to the Gasserian ganglion.

(Published in Acta Ophth., Jap. 63:3794 & 3802, 1959 in Japanese.)

Fig. 4. (C) N. Oculomotorius (Silver stain).

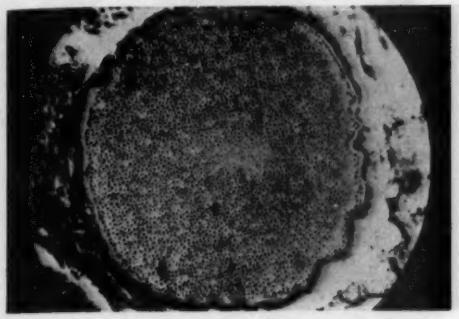


Fig. 5. (E) N. Trochlearis (Silver stain).

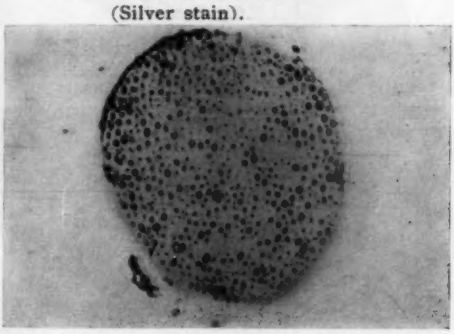


Fig. 6. (G) N. Abducens (Silver stain).

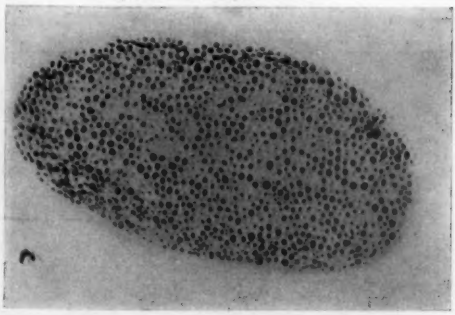


Fig. 7. (D) N. Trochlearis (O_3O_4).

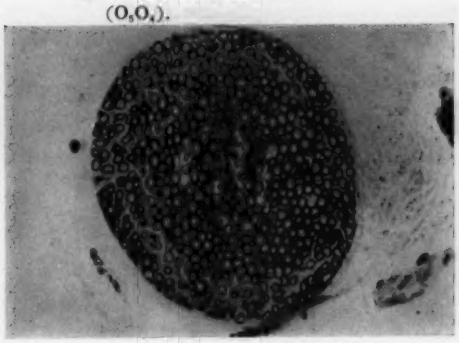


Fig. 8. (E) N. Trochlearis.

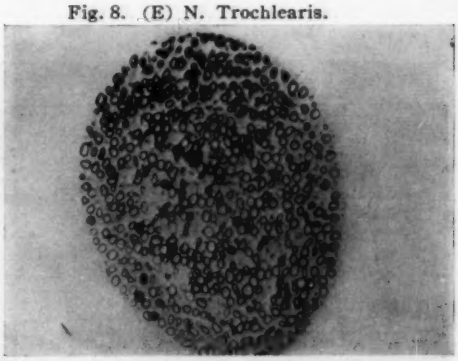


Fig. 9. (F) N. Trochlearis.

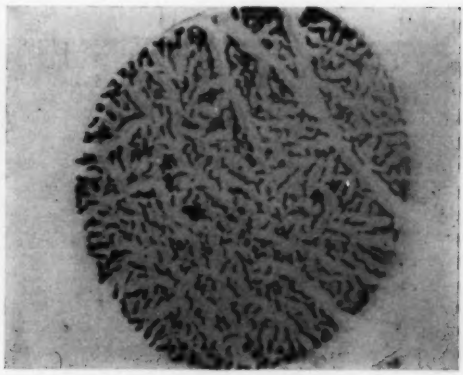


Fig. 10. (G) N. Abducens.

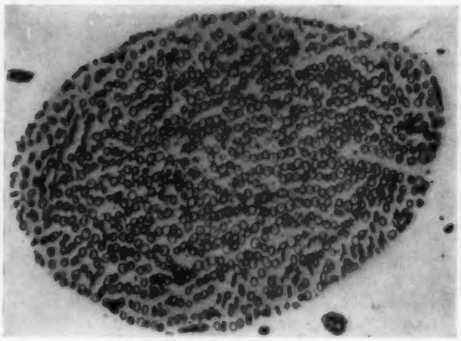


Fig. 11. (H) N. Abducens.

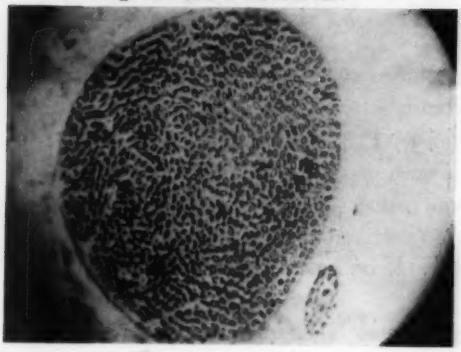


Fig. 12. (I) N. Abducens.

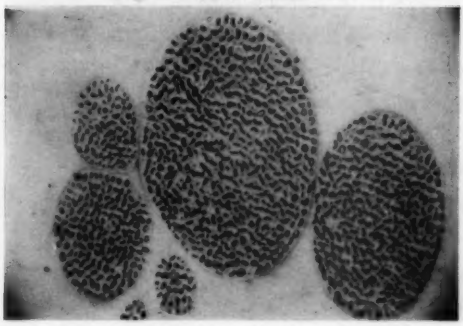


Fig. 13. (C) N. Oculomotorius.

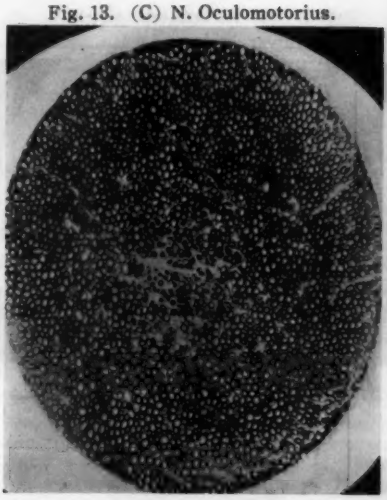


Fig. 14. (A) R. Sup, of N. oculomot.

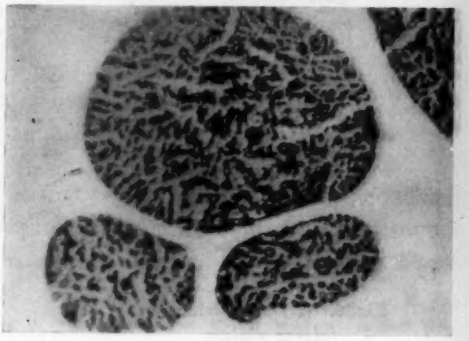


Fig. 15. (B) R. inf of N-Oculomot.

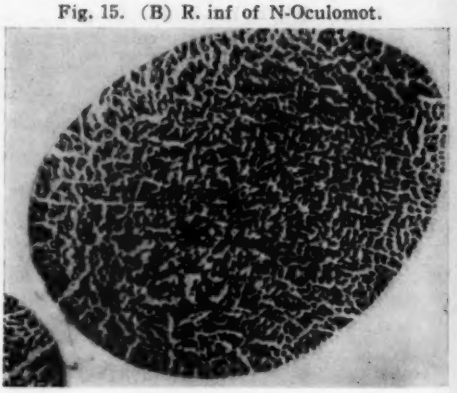


Fig. 16. (C) N. oculomotorius (high magnification).

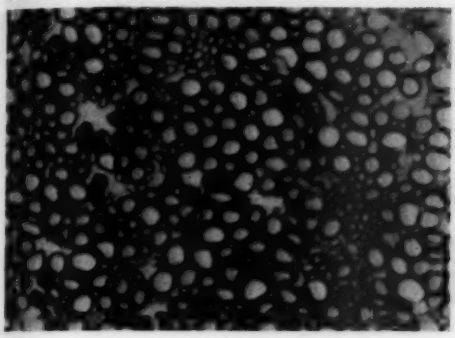


Fig. 17. N. Trochlearis (before the union).

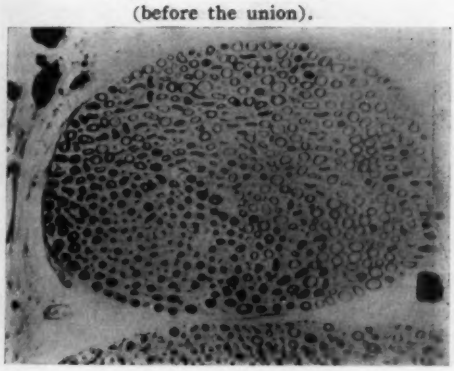


Fig. 18. N. Trochloaris (after the union)

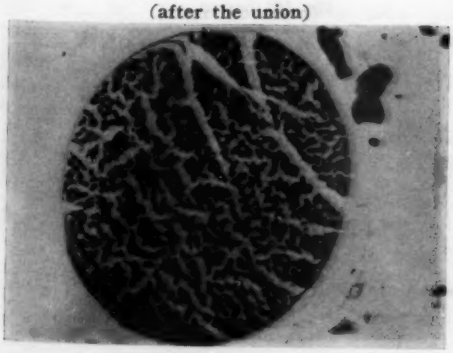


Fig. 19.

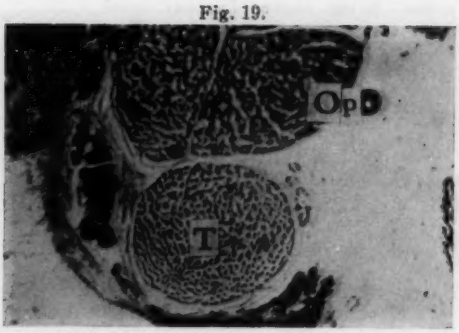


Fig. 20.

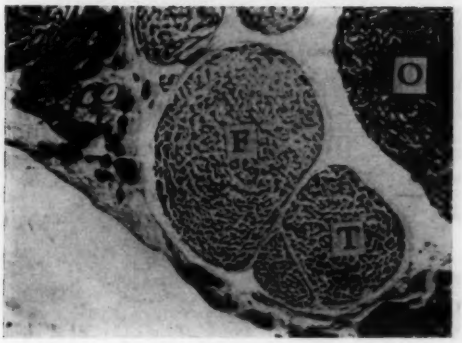


Fig. 21.

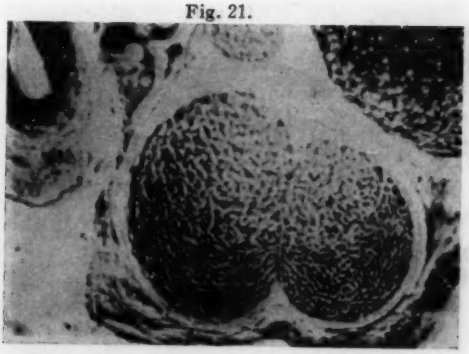


Fig. 22.

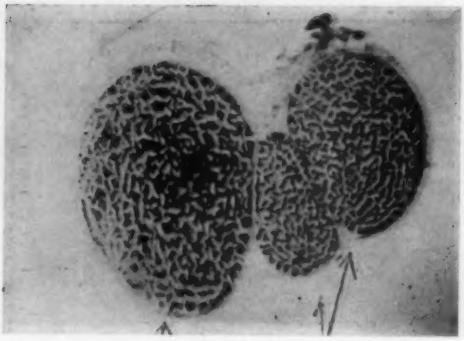


Fig. 23.

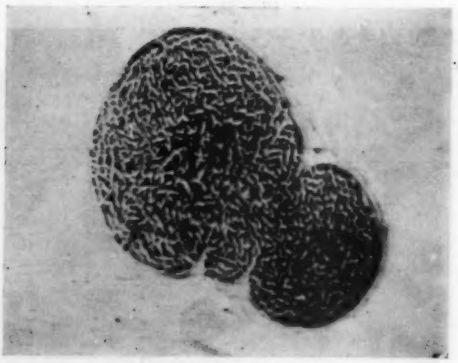


Fig. 24.

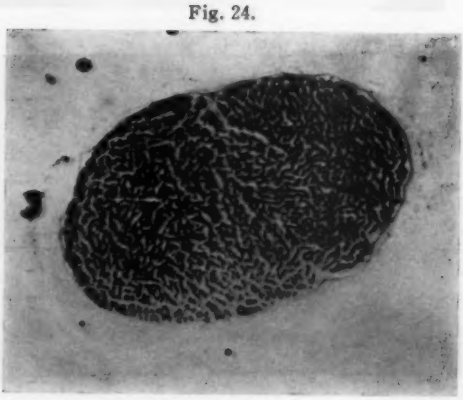


Fig. 25.

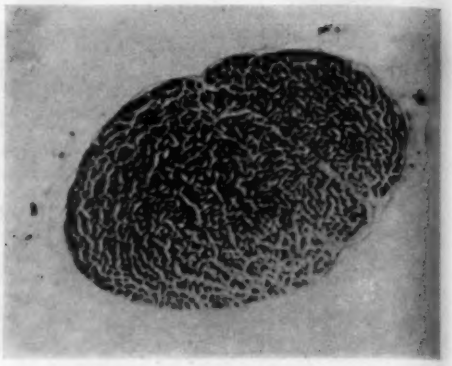


Fig. 26.

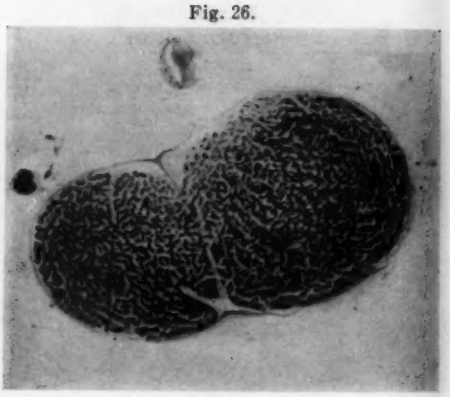


Fig. 27. Degenerated fibres in the 4th nerve.

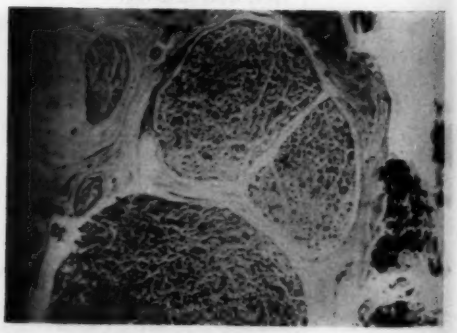


Fig. 19-25. Photo to show the process of the union between N. Trochlearis and N. Frontalis.

Fig. 28. Mutual anatomical relation of the ocular nerve.

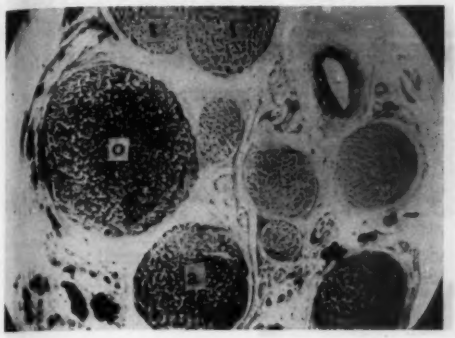


Fig. 29. Superior oblique muscle fibres.

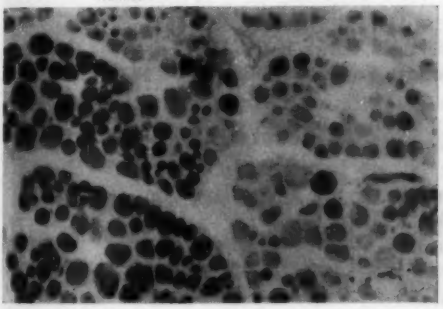


Fig. 30. Ganglion cells along the sixth nerve.

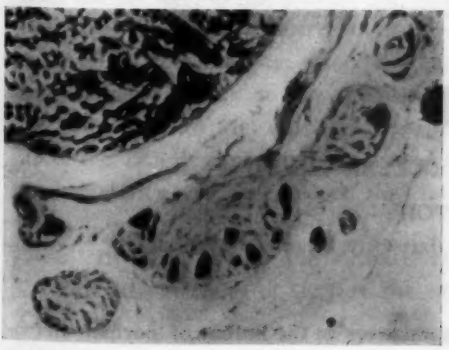


Fig. 31. The Ganglion cells receive fibres from the ophthalmic nerve and sympathetic nerve.

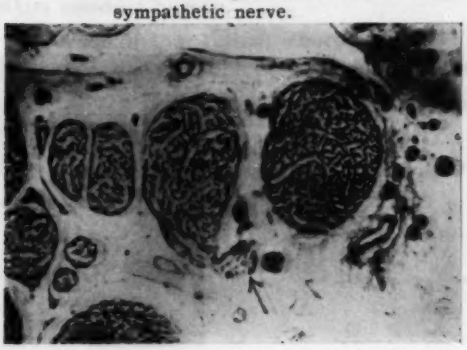


Fig. 32. Ganglion pterygopalatine.

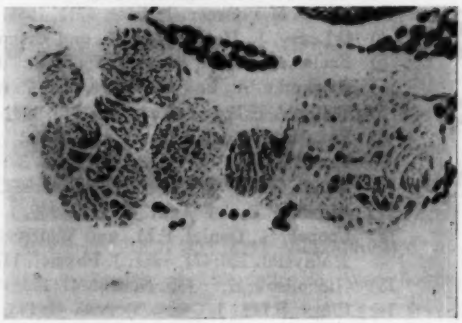


Fig. 33. Communication with the Ganglion pterygopalatine.

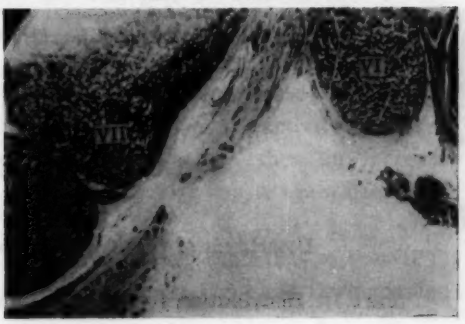
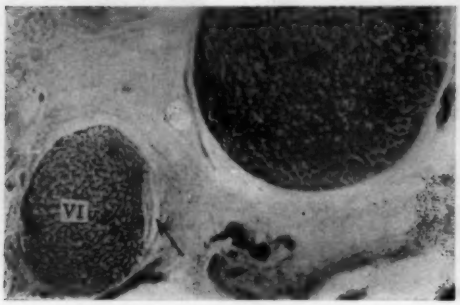


Fig. 34. Arrow shows the sympathetic fibers in the perineulium of the sixth nerve.



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TRANSAMINASES IN OCULAR TISSUE

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Part 1. Distribution in Normal Bulbus

The distribuion and activities of the transaminases in the bulbus of normal albino rabbits were determined using the method reported by Tonhazy, White, Umbreit et al.

1) The activity of the GOT decreased in the order of the retina, choroidea, iris and ciliary body, cornea, crystalline lens, and the aqueous humor.

2) The activity of the GPT decreased in the order of the retina, choroidea, iris and ciliary body and aqueous humor, however it was impossible to determine its activity in the cornea and crystalline lens.

3) When the activities of both the GOT and GPT were compared, the GOT displayed the higher activity in all parts of the bulbus except the aqueous humor. In the aqueous humor the activities of both were practically equall

GOT/GPT

liver: 22/1 retina: 12.8/1 choroidea: 8/1

iris and ciliary body: 3/1

4) Comparison with both the activities in the liver

GOT: liver/retina 3.3/1 liver/choroidea 5.7/1

liver/iris and ciliary body 15/1

GPT: liver/retina 1.9/1 liver/choroidea 2/1

liver/iris and ciliary body 2.3/1

Part II. Fluctuations in Both the Activities during the Process of Ocular Growth in the Chicken Embryo.

Using the embryo of albino leghorns, the activities of the transaminases were determined in the retina, choroidea, brain and liver on the 9th, 13th, 15th, 18th and 21st day during incubation and on the 1st day after birth, respectively.

1) The activity of the GOT gradually increased in the retina, choroidea, brain and the liver from the first day of incubation up to the 15th day and then showed a temporary decrease on the 1th day; however, the recovery of the activity was soon observed. These changes show parallelism to the fluctuation in the amounts of free amino acid and the activity of d-amino acid oxidase found in the retina of a chicken embryo.

2) The activity of the GPT in the reina and the choroidea gradually increased from the 1st day of incubation up to the 15th day, but then showed decrease on the 18th day and a further decrease on the 21st day. In the brain the lowest activity was observed on the 13th day, after the 13th day the activity showed a gradual increase and attained its peak on the 18th day, then it showed a slight decrease on the 12st day, but after the 21st day again increased slightly. In the liver the activity increased up to the 15th day, showed a temporary decrease on the 18th day, then an increase in the activity was observed on the 21st day but after the 21st day it again decreased slightly.

3) In every tissue the activity of the GOT was higher than that of the GPT.

Part III. Activity of GOT in the Retina of the Frog under Light-and Dark-adapted Conditions.

(experiments on the entire retina, the outersegment of the rod and the part of

the retina remaining after the outersegment of the rod had been removed)

Using frogs (rana esonlenta) which had been dark adapted for from 4 hours to thirty hours, the activities of the transaminases were determined on the entire retina after it had been stripped from the bulbus, the outersegment of the rod after it had been separated from the retina by Kimura's method and the part of the retina remaining after this separation, in each case the organic material was homogenised; the above operations all having been performed in the dark room.

Results were as follows; the activity of the GOT

1) in the entire retina light-adapted>dark-adapted

2) in the outersegment of the rod light-adapted<dark-adapted

3) in the part of the retina remaining light adapted≥dark-adapted

Here "light-adapted" means that the organic material was irradiated with a 300w. white electric bulb and "dark-adapted" means that no such irradiation occurred.

Part IV. The Activity of the GOT in the Retina after Insertion of an Iron Nail into the Vitreous Body of Albino and brown Rabbits.

The activity of GOT in the retina of albino and brown rabbits which had an iron nail inserted into the vitreous body of their eyes was determined on the 2nd, 4th, 6th, 8th and 10th day.

1) The activity gradually decreased after insertion from the 2nd day up to the 6th or 8th day.

2) The greater the area of contact between the nail and the retina, the less the GOT activity was.

Discussion

1) The fact that, in case of normal albino rabbits, the high activites of the transaminases were observed in the liver, retina, choroidea, iris and ciliary body of these rabbits seems to be due partly to the specific function of these respective organs and partly to the nature of the cells which form them or to the pattern of their arrangement in each organ.

The existence of GPT in the cornea and crystalline lens could probably be proved by other methods.

2) In the ocular development of chicken embryos the fact that these enzymes activities in the retina and choroid change in parallel with rise and fall of free aminoacids and d-aminoacid oxidases might indicate that assuming the free aminoacids continue to be accumulated in the retina until around the 15th day and the activities increase as they take part in synthesis and analysis and then they become low as the aminoacids are consumed around the 18th day.

3) As to the changes of light and darkness, we could not study the influence upon the pigment epithelium, as we used the darkadapted retina. Hayano report-

ed that the composition of aminoacids in retina is 10% more in quantity in the light than in the dark condition and that aspartic acid and glutamic acid are in smaller quantity in the light than in the dark-adapted condition. The activity of GOT in all the layers of the retinal tissue is remarkably higher in the light, for this reason we might suppose that the consumption is larger though aspartic and glutamic acids are composed in the light-adapted retina.

Both ATP-ase (Majima) in the outer segment of rod cells and dehydrogenase (Nitta) show higher activities in the light than in the darkness.

4) In the experimental siderosis bulbi, the activity is relatively higher in these cases in which an iron nail was penterated into the crystalline lens and laid in the vitreous body with the adhesion on the scleral wound of penetration. While on the other hand, it is less active in the cases in which stuck nail stayed in the vitreous body just touching the retina at its end or away from if. The larger is the space in which the iron touches the retina, the stronger are the siderotic changes. The degree of siderosis bulbi does not depend uopn the chemical quality of the iron used, but upon the size or other physical factors. It is said that siderosis occurrs in a horizontally radiated form around the iron and does not prevail farther through the vitreous body (Makiuchi). It proves that there exist lymphatic flow in the vitreous body from forward to backword.

By injecting "ferrobalt", into the vitreous body of albino rabbits macroscopic pigmentations were recognised at iris, conjunctiva, crystalline lens and vitreous body witeout suppurative infection up to the 35th day, only with a few exceptions. Around the 35th day retina displayed adhesive alterations. Retinal changes could not be observed by diaphanoscopy through darkened vitreous body due to the ferrobalt injected. Low activity was recognised in the few cases with suppurative infection.

Conclusion

1. Distribution in normal bulbus. (Table 1~7.)

a) Activity of GOT more decreased in the ordes of retina, choroid, iris and ciliary body, cornea, crystalline lens and aqueous humor.

b) Activity of GPT more decreased in the order of retina, choroid, iris and ciliary body and aqueous humor. In the cornea and crystalline lens, it was impossible to be determined.

c) When both activities were compared, GOT was higher than GPT. In aqueous humor both activites were almost equivalent.

d) Activity was high in the liver, retina, choroid, iris and ciliary body, but it was low in the cornea and crystalline lens.

2. Fluctuation on ocular growth of the embryo of the chicken. Activity of GPT increased in the retina and choroid from the beginning of incubaiion. It reached to a

peak on the 15th day, dropped on the 18th day, dropped further on the 21st day, then slightly rose again.

RESULTS

Table 1. GOT (Albino rabbits) u/g

	Liver	Retina	Choroidea	Iris & ciliary body	Aqueuus humor	Lens	Cornea
Mean	207600	41858	23800	13367	21.3	2875	3650

Table 2. GOT (White-black rabbits) u/g

Retina	Choroidea	Irs & ciliary body
90875	44200	33500

Table 3. GOT (Black rabbits) u/g

	Retina	Choroidea	Iris & ciliary bydy	Aqueous humor
Mean	66725	27005	14575	22,5

Table 4. GPT (Albino rabbits) u/g

	Liver	Retina	Choroidea	Iris & ciliary body	Aqueous humor
Mean	9333	67000	4617	4100	22

Table 5. GPT (Black rabbits) u/g

	Retina	Choroidea	Iris & ciliary body
Mean	2400	6600	2350

Table 6. GOT/GPT (Albino rabbits) u/g

	Retina	Choroidea	Iris & ciliary b.	Aqueous h. Liver Lens
GOT/GPT	10.8/1	8/1	3/1	

Table 7. GOT u/g

	Retina	Choroidea	Iris & ciliary body
Albino rabbits	63750	36000	13800
White-black	90875	44200	33500
Black	102250	48750	
Albino rabbits	17500		12750
Brown	25400		
Black	31200		14400

3. Activity of GOT in the retina of the frog under light or dark condition (Table 9).

Table 8. GOT in the Retina of Rabbits which have an Iron Nail Inserted into the Vitreous Body of their Eyes u/g

No. of Days	Albino rabbits	Brown rabbits	Black rabbits
Control	21480	35120	8580 (the 1st day)
2	23750	24930	22500 (the 3rd day)
4	21900	30440	46070 (the 4th day)
6	16230	24950	
8	12910	23080	
10	27030	22400	
15		24000	

Table 9. The Difference of GOT in the Outersegment of Rod and the Remained Retina of Frogs (rana esenlenta) between in the Light- and Dark-adapted Condition

Outersegment of rod			Remained Retina		
Wt. of dried material.	Activity in 1. mg of dried material.		Wt. of dried material	Activity in 1. mg of dried material	
	Light	Dark		Light	Dark
Mean 2,064	13.09	12,21	1.923	15.33	13,09

a) Entire retina; light>dark

b) Outersegment of rod; light<dark

c) Remained retina; light≧dark

4. Activity of GOT in the retina after the penetration into the vitreous body by a nail (Table 8).

a) The activity generally decreased from the 2nd day to the 6th—8th day, on both of the albino and brown rabbits

b) The wider area to contact with the retina the nail had, the more the activity became low.

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STUDIES ON GENETIC CARRIERS OF PROTAN TYPE OF COLOR VISION DEFECT

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In clinical genetics many investigations have so far been made on how to detect so-called genetic carriers and some manifest characters of them have been found in several kinds of hereditary diseases. A genetic carrier, according to Neel, means one who is symptomatically quite nomal or only slightly abnormal but yet possible to transmit the hereditary characters. Since those manifestations so far clarified are not peculiar to the carriers, it is yet almost impossible to distinguish carriers only by the manifest deviations from the normals without pedigree analysis.

As to the heredity of color vision deficiency, Neel[1] defines that a carrier is a female who might be defective in color vision to the least extent. Wieland, Schmidt, Walls, Crone and others have been investigating this problem but have not reached any definite conclusion. In Japan either, little is known on this question, to which more attention should be paid. We measured relative spectral sensitivity in long wave-length with heterozygous females selected from the families in which protano-defective children were checked up at the ordinary color viaion tests. We found that they showed rather notable deviation from the normals and we feel confident that this method is quite significant for the hereditary study of color vision deficiency.

Method

For the measurement of relative spectral sensitivity the specially deviced colorimeter was used which was modified from the anomaloscope Nagel II type as Crone[2] showed in his previous report. Relative spectral sensitivity was measured at the wave-length of 643.8 mμ (red light) and it is the reciprocal of these measured values in the revolver scale of the apparatus which mean stimulus threshold. As to the structure of the apparatus made up of a monochromomator and a flickerphotometer, Ichikawa[3] ,one of the authors, previously described. The mean normal values and distributions were

studied with 213 color vision normal school children over the 3rd grade who were diagnosed as normal in the test with the aid of Ishihara plates. The same examination with this flickerphotometer was given also to the mothers, might-be heterozygotes, of the subjects with protan type of color vision deficiency checked up at the customary tests with the pseudo-isochromic plates and anomaloscope. Besides, two other heterozygous females from the family in which a protano-defective subject was detected, were examined. Sixteen protano-defectives and 8 deutero-defectives also underwent this examination for the sake of comparison. Though this test had better been performed in the dark room, we did at the dark corner of the room, almost without any serious difficulty in management nor any unreliability of response given.

Results

The mean values of both the lower and upper limits in slit-scale with the 213 seeming color normal girls, for we can not deny this group never contain any carrier, are as follows; lower limit: 12.714, σ 1.309, upper limit: 13.639, σ 1.081, rejection interval of 1% being $16.117 \geq m \geq 9.311$ at the lower limit and $16.450 \geq m \geq 10.828$ at the upper. In this group were two girls who showed abnormal responses deviated from the normal value; one was in the third grade showing 12.8—19.0 and the other fifth grade girl 17.0—17.0. With critical ratio of 1% only the upper limit value in the former case was abnormal and both the upper and lower limits were abnormal in the second case. Thus, one of 213 females (0.47%) can be considered as abnormal, a might-be heterozygote and two of 213 (0.94%) were probably abnormal. The pedigree analysis of these two cases are now under study to ascertain if they are really genetic carriers or not.

Next, 10 proto-heterozygotes who were assured from the pedigree analysis were given the same examination, with the result shown in Table 1. Comparing the results with the average normal values shown before, in regard to the lower limit 6 of 10 showed abnormal responses, 3 within normal, 1 uncertain and in regard to upper limit, 8 abnormal, 1 normal and 1 unclear. With consideration of rejection interval of 1%, We adopted the value of lower limit as a criterion of abnormality, with the upper one only as a reference. Concluding from the facts mentioned above, 60% of proto-heterozygous females who were diagnosed as normal both with the pseudo-isochromic plates and anomaloscope showed abnormality in this examination. The result of the same examination with 16 subjects with protan type of color vision defect are shown in Table 2. They showed some degree of relatively clear deviation in high frequency from the normal and the deviations were larger than those shown by heterozygotes. In other words proto-heterozygotes lie between the normals and color vision defectives with slight overlap with the normals. The previous report by Ichikawa that the

heterozygotes of deutan type of color vision defect show some extent of deviation from the normal has no contradiction against the results in our experiment concerning the proto-heterozygotes.

Discussion

The characters of genetic carriers are mostly unclear, for the extent of deviations, carriers show, is not always remarkable, but often only in high frequency, but Neel reported 34 diseases in which the genetic carriers are more or less clarified. Among them are gout, familial hemolytic jaundice, keratosis spinolosa, spherocytic anemia with jaundice, sex-linked hypochromic anemia, sickle cell anemia, thalassemia major, xerodermia pigmentosum, xanthoma, acatalasemia and so on. It is interesting that

Colrr Vision Defectives						Heterozygous Females			
Name	Age	Sex	Type	A.Q.	Flicker Values	Relation-ship	No. of Ishihara Plates misread.	A.Q.	Flicker values
K.I.	6	♂	P	0—∞	18.2—20.0	Mother	0	1.0	16.5—17.0 (+)
K.Y.	7	♂	P	0—∞	18.6—23.0				
S.	11	♂	P	0—∞	21,5—24.5	Mother	0	1.0	18.5—22.0 (+)
A.	11	♂	P	0—∞	20.0—39.0	Mother	0	1.0	12.5—22.0 (±)
N. *	11	♂	P	0—∞	45.0—47.0	Mother	0	1.0	13.0 (—)
K.	8	♂	P A	0.75—0.27	12.0—19.0	Mother	0	13.5—0.75	17.8—18.0 (+)
S.	8	♂	P A	0,4—0,27	×	Mother	0	1.0	14.0—19.0 (±)
U.	8	♂	P A	0,75—0.16	50 ?	Mother	0	1.0	32 ?
N.K.	11	♀	P A	0,4—0,27	36.0—37.8	Mother	0	1.3—1.2	18.0—25.0 (+)
N.M.	10	♀	P A	0,56—0.27	27.0—32.0				
U.	9	♀	P A	(Hioki)	18.0—18.5	Mother	0	1.0	17.0—18.0 (+)
M.	45	♂	P A	0.45—0.27	23.0—25.0	Eldest daughter	1	1.1	18.0—20.0 (+)

Table 1. The Results with the Color Vision Defectives and the Heterozygous Famales from Their Families

Note: Flicker values representing the revolver scales of the monochrom-collimator.

genetic carriers of "acatalasemia" show a diminished amount of catalase, in high frequency. In the ophthalmology anophthalmos, degeneratio pigmentosa (sex-linked form), color vision defeciency, myogenous muscular atrophy (cataract), infantile form of amaurotic idiocy, Laurence-Moon-Biedl syndrome, myopia, xerodermia pigmentosa, (conjunctival changes) have been studied in regard to the carrier states. Among them the characteristics of a carrier of degeneratio pigmentosa are relatively well studied (Geoblad), while in others they are not certain enough. So far as it is concerned with color blindness, we can merely find such a description that a carrier is a female whose color vision is abnormal to the least extent.

As to the investigation regarding the abnormal characters of genetic carriers in color vision deficiency, Waaler (1927)[5] reported that they misread many of the Ishihara Plates. In 1933 Wieland[6] stated that proto-heterozygotes showed decrease in saturation discrimination for red light (long wavelength) with " Stufenphotometer " modified by himself, and the rise of the threshold value for the red light is 40% and for green 11—12% and that all of them were poved normal in anomaloscopic examination. The adjustment range of Rayleigh equation in anomaloscope had no any particular connection with the increaesed threshold for the red and green. This fact has generally been admitted by Engelking. Schmidt[7] measured the relative spectral sensitivity of the proto-heterozygotes with a Flickerphotometer by Beckstein and with a monochromomator by Leiss concluding that their luminosity curve had a shift to the short wave-length and lie between that of the normal and protano-defective subject, although

Name	Age	Sex	Type of color vision defect	A.Q.	Flicker Values
K.I.	6	♂	P	0—∞	18.2—20.0
K.Y.	7	♂	P	0—∞	18.6—23.0
S.	11	♂	P	0—∞	21.5—24.5
A.	11	♂	P	0—∞	20.0—39.0
N.	11	♂	P	0—∞	45.0—47.0
S.	11	♂	P	0—∞	24.5—27.0
S.	10	♂	P	0—∞	32.5—60.0
K.	8	♂	P A	0.75—0.27	12.0—19.0
N.K.	11	♀	P A	0.4—0.27	36.0—37.8
N.M.	10	♀	P A	0.56—0.27	27.0—32.0
U.	9	♀	P A	(Hioki)	18.0—18.5
M.	45	♂	P A	0.45—0.27	23.0—25.0
S.	10	♂	P A	0.56—0.40	21.9—31.0
T.	10	♂	P A	0.56—0.27	21.0—46.0
A.	10	♂	P A	0.27—0.16	21.5—25.0
A.	30	♂	P A	0.29	31.0—34.0
S.	38	♂	D	0—∞	5.0
N.	50	♂	D	0—∞	8.0—10.0
S.	31	♂	D	0—∞	7.0—8.0
S.	34	♂	D A	4.7—3.7	9.0
N.	33	♂	D A	4.3	7.0—8.0
T.	34	♂	D A	4.7	9.0
K.	28	♂	D A	4.3—3.2	8.0—8.5
M.	54	♂	D A	4.3—3.8	10.0

Table 2. The Relative Spectral Sensitivities for Red Light with Color Vision Defectives

they showed no abnormality in the customary color vision examinations. This phenomen is regarded as peculiar to a carrier, which was later called " Schmidt's sign " by Walls[8]. Schmidt reported the heterozygous females show normal response in the

anomaloscopic examination but show an enlargement in the equation range in their fatigued condition. Pickford (1944, 47, 48)[9][10] noticed that a heterozygote showed no deviation from the normal Rayleigh equation but enlargement of equation range in his study with "the rotating disk experiment", but a female with such an enlargement showed no tendency of decrease in relative spectral sensitivity for the red.

Walls and Mathews (1952)[11] found a heterozygote proved normal in the ordinary color vision tests showed the lowering of relative spectral sensitivity for the red, which was called "Schmidt's sign". Protoheterozygous females different from protanodefectives who are lack of the receptor for the long wave-length light, have abnomal perception of long wave-length light due to the defect of the conduction pathway from the receptor to what is called "brighness pool", thus Schmidt's sign coming out. Therefore, chromatic sensation is normal in structure and they suggested "branched pathway hypotheses" with the scheme of color perception for physiological analysis of Schmidt's sign. Schmidt (1955) supported Walls' hypothesis. De vries[12] (1948) pointed out that both a protoheterozygote and a deutero-heterozygote showed abnormality in luminosity curve. Crone (1959) measured relative spectral sensitivity at the V (530 mμ)/V (650 mμ). He reached the conclusion that is similar to De Vries' one. Moreover, he stated that protoheterozygotes have abnormality in higher frequency than deuteroheterozygotes. Crone[13] also said the genetic carriers showed the enlargement of Rayleigh equation in an amomaloscopic examination and that they often misread more Ishihara plates than normals do. We measured the relative spectral sensitivity for red light of 643.8 mμ wave length with the school girls. The purposes of our investigation are to obtain the range of normal group, to learn to what extent it is possible to check up a heterozygote naturally mixed up in the group and thirdly to study how different is relative spectral sensitivity of the pedigree-analised carriers from that of normals.

As the results of our investigation showed, the distribution of the measured values are rather small or in other words a relatively small spread of indivisual difference at the long wave length, and therefore, this method is rather profittable for the detection the carriers.

Two of 213 girls who underwent this examination showed decrease in relative spectral sensitivity, (one of them uncertain). But it is not certain whether they are really heterozygotes or not, for the lack of pedigree analysis which is now under study. It might be possible that some other heterozygous females, besides these two, without "Schmidt's sign" might be comprised in this group. We can caliculate theoretical percentage of the genetic carriers from the frequency of color vision deficiency so long as it follows the pattern of sex-linked recessive inheritance. Da being 5%, D,P and Pa 1% respectively, protano-carrier thus should be $\frac{p}{p+d} \times 2a\,(100-a) = 0.0098$ (0.01) that is about 1%. In our investigation 2 to 3 of 213 subjects might be contained. The frequency of the might-be heteros in our experiment is rather near to this

calculated theoretical value.

Next, the same test was given to the ten genetic carriers determined from the pedigree study, the decrease of lower limit was proved in 60%. We might say the decrease of the lower limit of relative spectral sensitivity for red light be a charactor istic of a protoheterozygote when compared with the low frequency of 0.94% of abnormality among the normals.No tendency of misreading Ishihara plates and no enlargement of Rayleigh equation in anomaloscopic examination were recognised.

Two cases with * in Table 1. were given many kinds of color vision tests. One of them showed normal spectral sensitivity and no any abnormality in all other kinds of examinations, and the other showed a clear Schmidt's sign but made only one misreading in Ishihara plates, making no error at all in H-R-R test, Tokyo College of Medicine plates test, anomaloscopic examination and contrast test. In other words, the second one is a heterozygote who showed abnormality only in relative spectral sensitivity but otherwise quite normal. It is not doubtful from Pickford and Crone that a proto-heterozygote with Schmidt's sign shows a decrease both in hue discrimination and saturation discriminaiton, but it can not be absolutely concluded that it is peculiar to a proto-heterozygote. Thus, we can safely say that a protoheterozygote shows abnormality in relative spectral sensitivity in high frequency and only a small possibility of abnormal responses in other color vision tests It is not defenite why such a heterozygous female shows normal response in anomaloscopic examination notwithstanding the abnormality in relative spectral sensitivity. With some new methods with more precise and complexed mechanism to test color vision, the effect of the changes in relative spectral sensitivity upon the color matching would be more elucidated. We don't admit Walls' hypothesis, for this has no morphological or anatomical basis, though it might be convenient to understand the Schmidt's sign. Though the abnormality of relative spectral sensitivity of protano-defecitves may appear similar to that of a heterozygote, the former shows distinguishable abnormality in the color vision tests on account of essential difference in saturation discrimination between the two.

To state the significance of measuring the relative spectral sensitivity as a color vision test especially with heterozygous females, it is an excellent method, for relative spectral sensitivity depends upon the perception of flickering, unrelated to color percepion and the fall of hue discrimination and saturation discrimination don'dt influence this test so much, and moreover it is easier and surer than any other method also for distinguishing protano-defectives from deutero-defectives. As our investigation reported here shows, the responses of normals lie in a rather narrow spread and no abnormality in response was given by any subject with normal color vision. For these reasons one who is normal in the color vision test with pseudo-isochromic plates and yet shows abnormality of relative spectral sensitivity can be

considered as a genetic carrier of color vision deficiency. Now that Schmidt's sign is the only characteristic that has so far been clarified concerning the genetic carriers, this method can be regarded as so important for the test of color vision defectives that it should be performed together with the customary examinations with pseudo-isochromic plates and anomaloscope.

Conclusion

With 213 color normal girls relative spectral sensitivity for red light of 643.8 mμ wavelength was measured with a colorimeter modified from an anomaloscope. One of 213 (0.47%) was considered as a heterozygote and another probably as a heterozygote. Thus, 2 of 213 (0.94%) might be regarded as heterozygotes for their abnormality in relative spectral sensitivity, though the pedigree analysis of them are under study.

The same examination was given to 10 proto-heterozygous females from the families in which protano-defective subjects were found, and abnormality was recognized in 60% in much higher frequency than among normals. All 10 proto-heterozygotes showed no abnormality in pseudoisochromic test plates and in Rayleigh equation of anomaloscope.

Regarding relative spectral sensitivity proto-heterozygotes lie between normal subjects and protano-defectives. From the facts above we could conclude that most of proto-heterozygotes show decreased relative spectral sensitivity for red light while some of them do not.

Thus, the measurement of relative spectral sensitivity as well as pseudo-isochromic examinaiton, would play an important role in the study of color vision deficiency, especially in the genetic investigation.

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NEW ELECTRONIC OPHTHALMODYNAMOMETER

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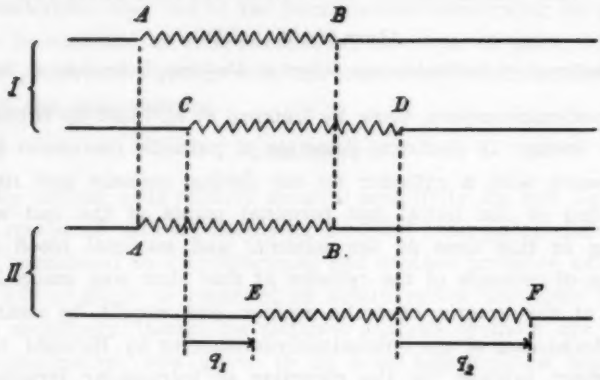
As ophthalmodynamometers, those by Uemura et al.[1] and by Hiroishi et al.[4] are available. The former is electrical detection of pulsatile movement of the cornea at the time of pressure with a cylinder on the limbus corneae and its neighborhood. With the handling of the initial and terminal points of the 2nd wave out of two waves appearing at this time as the minimal and maximal blood pressures respectively, addition of pressure of the cylinder at that time was made known and the blood pressure at the arteria centralis retinae was sought by means of the calibration line. Mechanism of the ophthalmodynamometer by Hiroishi et al. is almost the same. In short, process for the elevation of intraocular tension with the use of the electronic ophthalmodynamometer by Uemura et al. is nothing but a backward pressure on the eyeball. In these apparatuses, there is a freqnent appearance of corneal pulse wave resulting from an overlap of the pulsation of the ophthalmic artery on that of the intraocular artery[3][4].

According to an idea originated with the author, the eyeball is located in front of the cone-like orbit and the orbital wall is made up of hard osseous substances. At the rear of the eyeball there are a large number of adipose bodies with a formation of corpus adiposum orbitae, and although the adipose bodies are facilitating the movement of the eyeball, pressure on the eyeball from the front does not lead to an escape of the bodies into the front of the ball because of hindrance by the muscle, tendon, blood vessel, nerve, connective tissue and so on. In other words, it may be considered that pressure on the eyeball from the front can give rise to an elevation of the pressure within the orbit situated behind the eyeball. In the case when this intraorbital pressure becomes higher than the minimal blood pressure of the ophthalmic artery within the orbit, the ophthalmic artery begins to pulsate and the pulsation is transmitted by way of the supple corpus adiposum orbitae to the front eyeball. As regards the relationship between the intraorbital pressure and the intraocular pressure, the author's formula[5], that is,

$$p=p_0+\int_0^l t_1^*(x,\lambda)\frac{d\lambda}{r_1-\lambda}+\int_0^l t_2^*(x,\lambda)\frac{d\lambda}{r_2-\lambda} \qquad (1)$$

is formed. By p and p_0 are meant the intraocular and intraorbital pressures respectively and the two integrands on the left side are related to the tension of the sclera and the radius of curvature. Thereupon, when (1) is written as $p=p_0+q$, q becomes a term connected with the tension and thickness of the sclera and the radius of curvature, but since the scleral thickness and the radius of curvature in respect of one eye to be examined may be considered to be generally definite, q will be allowed to be regarded as a term concerning the tension of the sclera.

Fig. 1.



Needless to say, when p is raised by a simple pressure from forward on the eyeball, scleral tension is increased with the resultant increase of q, but as the eyeball as a whole is pressed toward the rear, p_0 is enhanced in line with the enhancement of p. In Figure 1, (I) is a model drawing of the blood pressure of intraocular and ophthalmic arteries, whereas (II) is the one displaying the relationship between the intraocular pressure p and pulsation at the time of bringing into existence the pulsation through simple pressure from forward on the eyeball. That is, as the intraocular artery is more peripheral than the ophthalmic artery, both minimal and maximal blood pressures (A,B) of the former are lower than the corresponding pressures (C,D(of the latter. Also, with respect to the pulsation, if the p value is between A and B in the instance of the intraocular artery, there is a pulsation of the artery. However, since q in the formula of (2) varies with the size of p, if q at the time of minimal and maximal blood pressures of the ophtqalmic artery is expressed as q_1 and q_2 respectively, pulsation in the instance of the ophthalmic artery is noticed when the p value is lying between $E(=C+q_1)$and $F(=D+q_2)$. Turning to the consideration of the process for the addition of pressure on the eyeball with gradually increasing intensity, pulsation of the intraocular artery begins with A and ends in B, whereas that of the ophthalmic artery starts with E and ceases in F. Fortunately, in case E is higher than B, pulsation of the ophthalmic artery begins after the termination of that of the intraocular artery, so the end-point of the pulsation of the intraocular artery can be known by the pulsation of the cornea. However, since transmission into the cornea of the pulsation of the ophthamic artery takes place as well, when B is equal to E or lies between E and F, there is a pile of the pulsation of the intraocular artery above that of the ophthalmic artery. Moreover, as there are ramifications of the ophthalmic artery in the orbit and the maximum and minimum blood pressures of these are lower than those of the ophthalmic artery, it should be considered that the possibility for the pile of the pulsation of these branches above that of the intraocular artery is

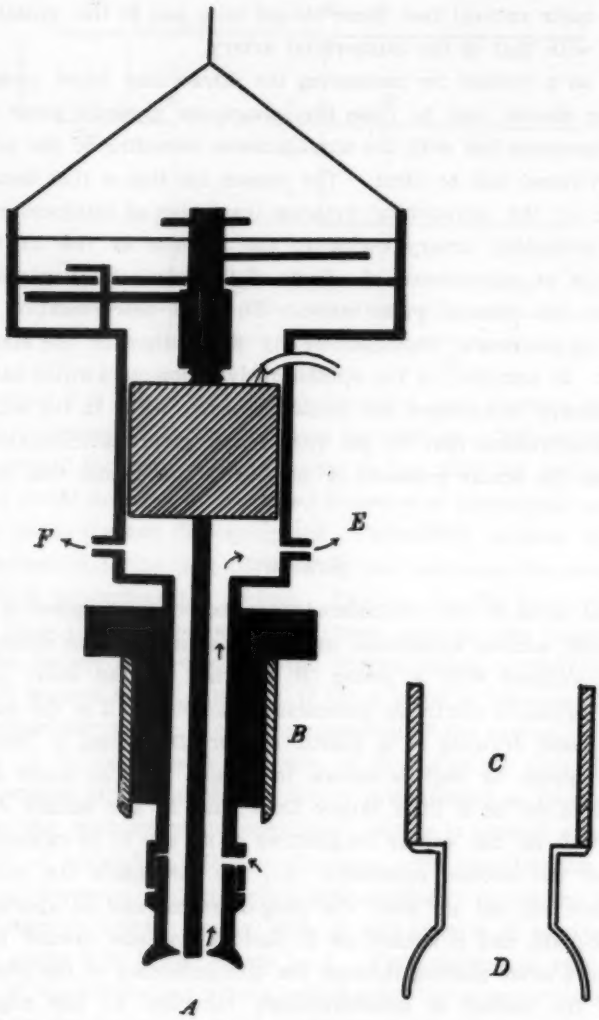
larger than in the case of the ophthalmic artery. On the basis of such consideration, it appears to be quite natural that there should be a pile of the pulsation of the intraocular artery with that of the intraorbital artery.

Accordingly, as a method for measuring the intraocular blood pressure with the use of recording sheets, one to raise the intraocular pressure alone without raising the intraorbital pressure but with the simultaneous recording of the pulsation of the intraocular blood vessel will be ideal. The reason for this is that because of absence of the pulsation of the intraorbital arteries (exclusive of intraocular artery) to say nothing of the ophthalmic artery owing to the absence of rise of the intraorbital pressure, there is no appearance of effects of the intraorbital arteries such as ophthalmic artery on the corneal pulse wave. To meet this condition was the main purpose of the experimental manufacture by the author of the electronic ophthalmodynamometer. In addition, in the ophthalmodynamometers which have hitherto been used, it is necessary to measure the initial pressure, while in the author's one, it is one of the characteristics that to get rid of the errors attributable to the above-mentioned proesss the ocular pressure is measured throughout the course of measurement.

Structure

The principal parts of this ophthalmodynamometer are composed of pick-up, sucker with piston cylinder, suction apparatus, suspension apparatus and recording apparatus. Pick-up (*A*) is furnished with a piston (*B*) attached on the lower part of that of Yamamori and Hayashi's electronic tonometer[6] and Figure 2 is the model drawing of this. Also, the model drawing of a plastic sucker (*D*) having a piston cylindr (*C*) adapted to this piston as well is shown in Figure 2. The inside diameter of this sucker is required to be a little larger than that of the sucker cylinder. This sucker is adsorbed on the ocular conjunctiva of an eye to be examined. By means of the starting of the suction apparatus (*E*), the air inside the sucker is inhaled through an orifice set set up near the plug-in region and an aperture between the plunger and foot-plate, and is sucked as it further ascends toward the direction of arrow in the figure after passing through the circumference of the plunger. Negative pressure inside the sucker is simultaneously recorded by the negative pressure-recording apparatus (*F*) on the recording sheet of the electronic tonometer. Figure 3 is a picture of the main portion of the electronic ophthalmodynamometer, and pickup. Figure 4 is a model drawing of the suspension apparatus in which the pick-up and a pan loaded with a weight kept in balance with the amount of heaviness of the pick-up and of sucker with piston cylinder are being suspended with a long steel wire on the both arms of a scale. Practically, this weight should be rendered 20 grams heavier than the amount under the balanced condition. This procedure is taken to stand against an appreciable power by the palpebra of an eye to be examined to press the sucker from

Fig. 2.



outside and push it down toward the posterior of the eye to be emamined. It is required to have the other eye of the subject fixed on the light for fixed vision (*G*). The left drawing in Figure 5 is a model one immediately before measurement by bringing the sucker into contact with the eyeball. Hereupon, when suctien is conducted, negative pressure is produced within the sucker and the pick-up descends and puts pressure on the eyeball. That is, the right drawing is a model one exhibiting the descent of the pick-up as indicated by an arrow mark at its center. Since the pick-up

Fig. 3.

Fig. 4.

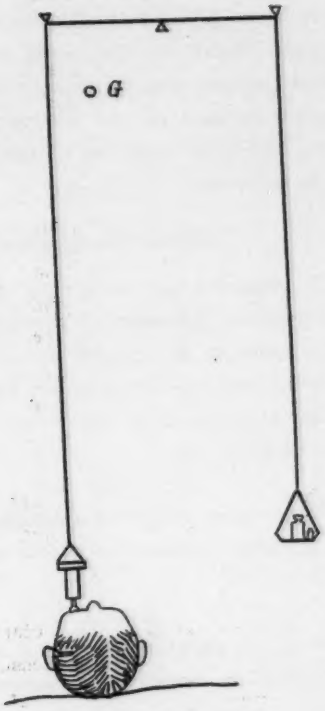
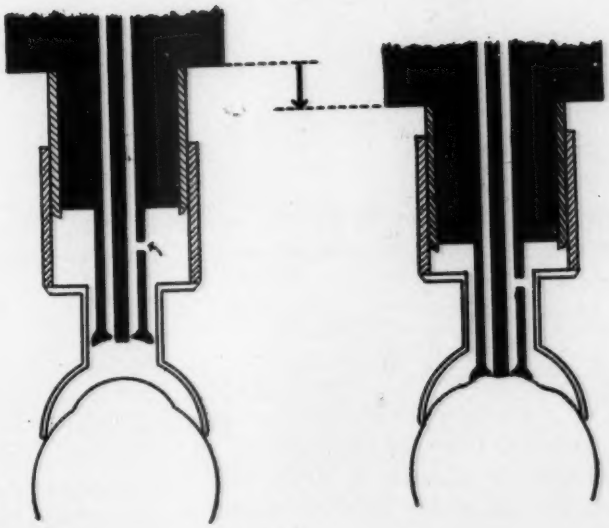


Fig. 5.



is kept in balance, through the arms of the scale, with the weight, the eyeball as a whole is not pressed at all toward the orbit, so there is no rise of the intraorbital pressure, However, the lower end of the pick-up is pressing both the cornea and limbus corneae, also the sucker limb is pressing the scleral region and the negative pressure is sucking the sclerocornea, so a transformation is made of the eyeball, giving rise to an elevation of the intraocular pressure. In other words, the desired end is schieved.

Method for obtaining the Value of the Intraocular Pressure

In obtaining the intraocular pressure (Pt mmHg) by the plunger load (W g) and negative pressure (N mmHg) inside the sucker, the following method is used. In the instance of putting pressure on the cornea by means of the footplate and plunger, with the intraocular pressure in the state of pressure as p, with the extraocular pressure as p_0 and with h as a constant, the following approximate formula is obtained[5].

$$p-p_0=hW \tag{3}$$

Thereupon, when the atmospheric pressure, negative pressure inside the sucker and pressure inside the sucker as extraocular pressure are expressed as A,N and p_0 respectively,

$$p_0=A-N \tag{4}$$

is set up. Also, as the intraocular pressure is usually manifested by the degree of height in which the pressure in the eyeball is excelling the atmospheric pressure, when the intraocular pressure during measurement is expressed as Pt,

$$Pt=p-A \tag{5}$$

is obtained.

From (4) and (5),

$$Pt=p-p_0-N$$

is resulted.

When (3) is substituted for this,

$$Pt=hW-N \tag{6}$$

is obtained. Determination of h in (3) with the unit of W as g, on the basis of the value for the reading of 5.0 and the plunger load of 10 grams in Priedenwald's Table in 1955, brings about h=5.682.

Accordingly, (6) becomes

$$Pt=5.682\ W-N \tag{7}$$

However, the unit of Pt and N is mmHg. By the way, what is in need of attention is that as the formula is brought into existence only with the presence of footplate load, (7) is generally established with $W>4$.

Let the author cite one example of computation and seek the maximum blood pressure when in the judgement point the height of plunger load curve was made

5.6 cm higher than that (base line) of plunger load curve at the time of plunger load =0, the dial then was set at the graduation of 3 and the height of negative pressure pen was made higher by 26 mm than that of negative pressure pen before the beginning of suction. Since adjustment was made in order that 1 cm of the movement of the plunger load pen might be equivalent to 1 gm of the plunger load and the dial is set at the 3rd graduation, the plunger load is 25.6 gm. Also, as it was adjusted that 1 cm of the movement of the negative pressure pen would be equivalent to 20 mmHg, the negative pressure is 52 mmHg. Therefore, the intraocular pressure *Pt* at this time is, through the formula of (7),

$$Pt=5.682\times25.6-52=93.5 \text{ mmHg}$$

That is to say, the maximum blood pressure is 93.5 mmHg.

Safeness of Measurement

The highest negative pressure within the sucker required for measurement is about 50 mmHg in the case of a normal eye and 100-150 mmHg is enough seven in a hypertensive eye. Up to the present, no case has been reported on the damage of the intraocular region. Since the lower end of the pick-up does not rub the corneal surface because of immobility of the sucker being sticked fast to the eyeball, no damage is inflicted upon the cornea. Anesthesia with eye drop alone is sufficient and the subject feels little or no pain. Moreover, there is no necessity for the administratisn of analgesic, nor is eye-wash necessgry on the following day. In any event, there is no fear of perceptible damage or pain being inflicted upon the eye to be examined, and the measurement can be made with extreme safety.

Experimental Case

An explanation will be made of an example (Figure 6). Since *N-N'-N* is a negative pressure curve and the negative pressure pen is being recorded at a location 32 mm later than the plunger load pen at the same time, it is expected that this matter will be kept in mind. Also, *C-C* is the first limb lead curve on the electrocardiogram and the electrocardiographic pen is being recorded at the identical location as in the plunger load pen at the same time. For the purpose of recording the plunger load of 0-60 gm, arrangement of an exceedingly wide record sheet is needed. Thereupon, device was made so that at each turn by one graduation of the dial of the recording apparatus the plunger load pen might be descended by 10 cm. Then, for example, by $D_1 \leftrightarrow D_2$ is meant the border between the 1st and 2nd graduations. Pressed corneal pulse wave makes its appearance from around *F*, followed by a gradual rise of the wave height, but the wave height is again diminished with a resultant disappearance and there is no subsequent appearance of the corneal pulse wave. Thus, an inevitable extinction of the corneal pulse wave is the distinct feature of this ophthalmodynamometer. Intraocular pressure at the time (*G*) of this extinction is representative

New Electronic Ophthalmodynamamometer (Akira YAMAMORI)

Fig. 6—1.

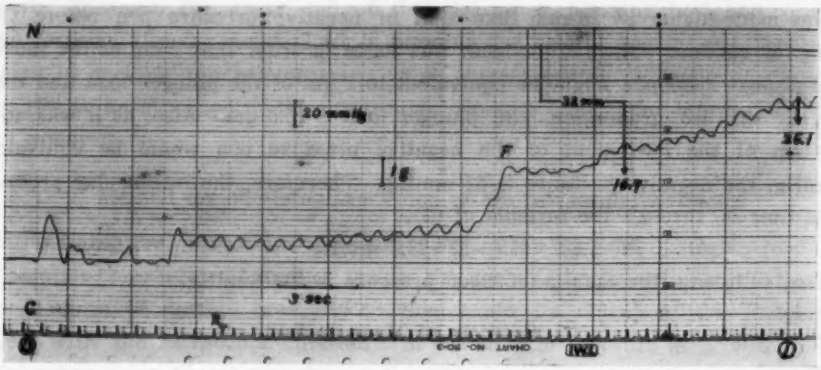


Fig. 6—2.

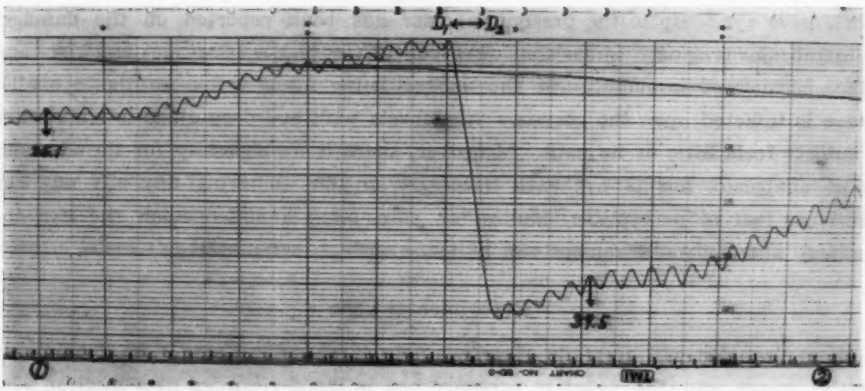


Fig. 6—3.

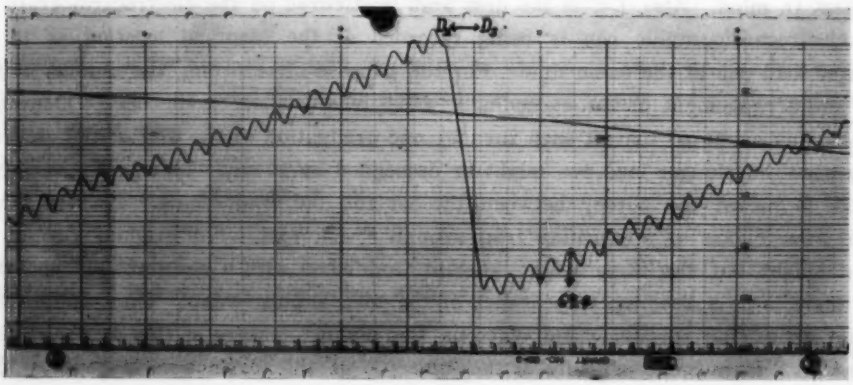


Fig. 6—4.

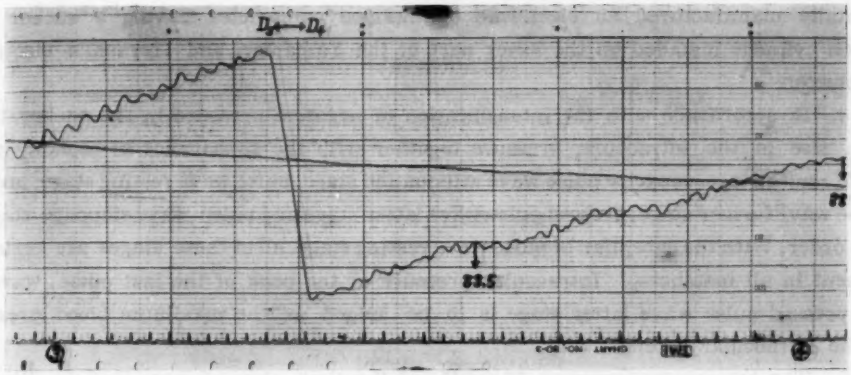
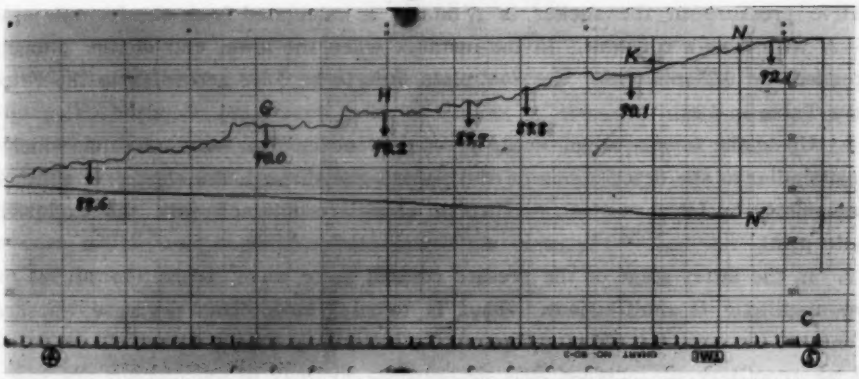


Fig. 6—5.



of the maximum blood pressure of the intraocular artery. By the way, in the vicinity of the judgement point for the maximal blood pressure, occasional appearance of several maximal blood pressure points such as *H* and *K* differing slightly one another in the value is considered due to a slight deflection by the passage of time of the maximal blood pressure of the subject.

Conclusions

1. Simple addition of pressure from the front on the eyeball gives rise to an enhancement of intraocular tension as well as intraorbital one. Consequently, as to the corneal pulse wave making its appearance at this time, a theoretical explanation that there is a pile-up in the pulse wave of component originating from the intraocular artery and that being derived from the ophthalmic artery was made.

2. Accordingly, in the measurement of the intraocular blood pressure by means of the recording of corneal pulse wave, an ideal method is to enhance the intraocular pressure alone without raising the intraorbital one and to simultaneously record the corneal pulse wave and intraocular pressure as well.

3. As an apparatus complying with the above conditions, the author experimentally manufactured an electronic ophthalmodynamometer having a sucker with piston cylinder installed on the lower part of the Yamamori and Hayashi's electronic tonometer.

4. In accordance with the intensification of negative pressure in the sucker, there is a rise in the intraocular pressure together with the appearance of capacity pulse wave zenith stage, capacity pulse wave attenuation stage, pulse wave resting stage, pressed pulse wave former stage, pressed pulse wave latter stage and pulse wave stoppage stage in this order. With the exceptian of pulse wave resting stage, all of these stages are certainly present in all instances. Intraocular pressure at the peak of the last pulse wave in the pressed pulse wave latter stage is to be judged as the maximum blood pressure of the intraocular artery.

5. The intraocular pressure Pt mmHg at the time when plunger load is Wg and negative pressure in the sucker is N mmHg is calculated from the formula of $Pt=hW-N$ with h as a constant. In the instance when the lower end of the plunger is descended by 0.25 mm from the foot-plate, h is to be 5.682 according to the Friedenwald's Table in 1955.

6. Up to the former stage of the pressed corneal pulse wave, results which are almost similar as the descriptions on the pulse wave through the electronic ophthalmodynamometer by Uemura et al. or Hiroishi et al. are obtained with the exclusion of minute point.

7. In the latter stage of the pressed corneal pulse wave, transition of the pulse wave amplitude is multifarious. That is to say, monotonous decrease, appearance for once of the maximal point, temporary continuation of an almost fixed value as well as repetition of increase and decrease on the way to monotonous decrease and in extreme instances transient stoppage of the pulse wave are observed.

8. In the majority of cases, a flat-bottomed pulse wave of peculiar form appears near the termination of the latter stage of the pressed corneal pulse wave exhibiting a gradual decrease in the wave amplitude with the resultant termination of the pulse twave stage. It will be adequate to describe the flat-bottomed pulse wave as being hat the bottom of the ravine of the pulse wave is flat and the declining wave amplitude is, figuratively speaking, a mountain disappearing below the surface of the water.

9. In the site bearing resemblance to the dicrotic protuberance observed in the radial artery, there is frequent appearance of an accessory peak in the pulse wave.

10. Since the intraocular pressure is being measured throughout the course of measurement, there is no need for measuring the so-called initial pressure as well as for using the calibration line. Hence, there is no mingling of the errors attributable to these procedures.

11. Measurement with this instrument is easy, the results are recorded with exactitude and there is no room for the mingling in the measured value of subjective views of the examiner, also as a collyrium alone for anesthetic purpose is put to use,

no pain is felt by the examinee, nor is there hazard of injuring the eye to be examined.

(Published in Acta Ophth. Jap. 64: 417, 1960 in Japanese.)

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DIVERGENCE EXCESS

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In divergence excess, extreme exophoria appears at the gaze of a far away place while orthophoria or only very mild exophoria is observed at the gaze of a nearly place. This disease has been paid attention to since the report of Duane, and discussed in relation with exotropia intermittens, or further, with the etiology of exotropia. The outline of this disease is discussed in this paper with a report on one case which was encountered in our clinic recently.

Case Report

A 18-year old normally born female. The patient appears to be slightly nervous, but has no history of a serious disease.

Her parents are healthy and normal ophthalmologically. There is no brother or sister. One of her cousins has developed exotropia intermittens.

Five years ago (when she was 13 years old), the patient noticed that the visual acuity of the left eye became poor and her parents observed outward deviation of the right eye at the gaze of a far away place.

On examination, the visual acuity was:

V.d.=0.05 (0.5×−10D)

= (0.8×contact lens)

V.s.=0.8 (1.2×−0.5D)

Exotropia was not observed in binocular fixation both at the gaze of a far away and a nearby places. (Fig. 1.A,A′)

The right eye markedly deviated outward at the gaze of a far away place when it was covered, but returned to the condition of binocular fixation, when the cover was removed. (Fig. 1.B)

However, the right eye did not show the outward deviation at the gaze of a near by place even when it was covered. (Fig. 1.B′)

Fig. I. Preoperation.

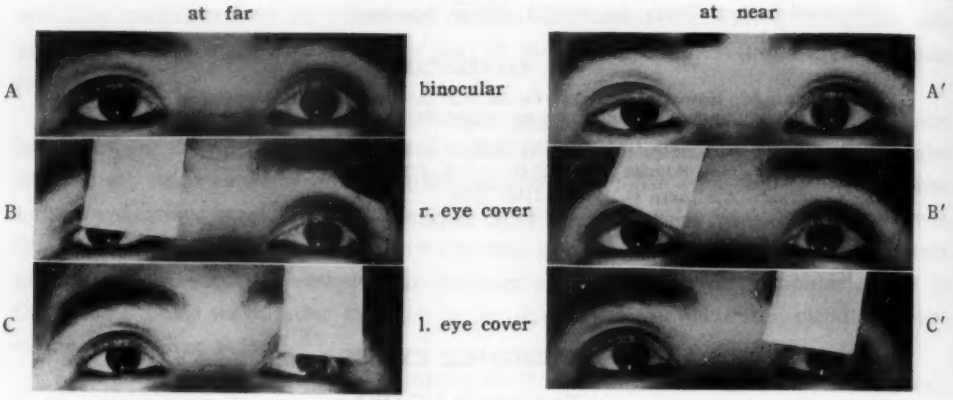
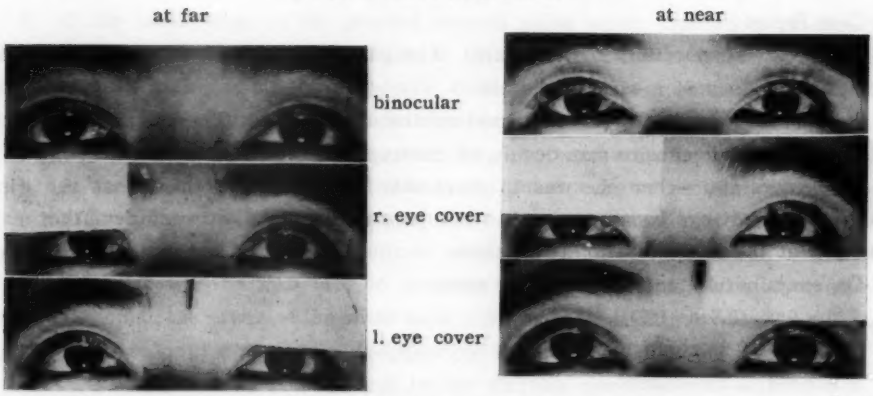


Fig. 2. Under general anesthesia.

Fig. 3. Post-3rd operation.



A similar phenomenon was observed, when the left eye was covered. (Fig. 1.C.C′.)

These results of cover test were unaltered when concave lenses were applied at the gaze of a far away place, when convex lenses were applied at the gaze of a near by place, or when homatropin was administered topically. Further, the outward deviation did not occur after covering the right eye for 24 hours.

Deviation angles of the exotropia were 25° at 5 m. and 2° at 30 cm. Vertical deviation of the right eye was strabismus sursumvergens of 3° at 5 m. and 2° at

30 cm., and that of the left eye was strabismus deorsumvergens of 4° at 5 m. and 3° at 30 cm.

Convergence near point: 8.0 cm.

Eye movements: normal.

Retinal correspondence tested by after-image method was in the normal range.

Prism divergence at 5 m.: 8°

Prism convergence at 5 m.: 7.5°

* Convergence-accommodation ratio "k"=1.01
* Accommodative convergence-accommodation ratio "A"=0.66
* Proximal convergence-accommodation ratio "P"=0.35 (Table 1.)

Table 1.

	Deviation angle		Prism-Divergence	Prism-Convergence	K.	A.	P.
	5 m.	30 cm.					
Preoperation	25° exo.	2° exo.	8°	7.5°	1.01	0.66	0.35
Post-2nd operaton	10° exo.	2° exo.	8°	9°	1.09	0.79	0.30
Post-3rd operation	0	5° eso.	2.5°	7°	1.18	0.92	0.26

K: Convergence-accommodation ratio
A: accommodative convergence-accommodation ratio
P: Proximal convergence-accommodation ratio

As I had stated in a previous paper, in normal subjects the "k", "A", and "P" are 0.80, 0.59 and 0.21 respectively. In this patient, "A" was almost normal while "P" was increased and accordingly "k" was much increased.

Therefore, I can conclude, that proximal convergence was larger than the normal value in this patient.

Operation

Recession of the m. lateral recti of the right eye by 5 mm. was performed under general anesthesia. Marked divergent position was observed under general anesthesia (Fig. 2), which was considered to be an anatomical resting position.

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* On the target of Hapoloscope, Landort's ring for one eye and a short line for the other eye were drawn. The scale, when the Landort's ring was superimposed on the straight line was read.
The target distances were 50 cm., 30 cm. and 14 cm. At each distance, correctional lens, +2D added lens and —2D added lens were 9 sorts of combinations altogether in the test condition.
The value at various target distance (no change lens) divided by 5D was taken as the convergence-accommodation ratio "k"; the value using various lenses (no change target distance) divided by 4D, as the accommodative convergence-accommodiation ratio "A"; and the difference between "k" and "A", as the proximal convergence-accommodation ratio was seen as "P".

The result of the cover test done 10 day after the operation was almost the same as that of the preoperative condition.

Recession of the m. lateral recti of the left eye by 5 mm. was made similary 14 days after the operation on the the right eye.

Clinical tests on the 19th day after the 2nd operation revealed; deviation angle: 10° at the gaze of a far away place and 2° at the gaze of a near by place; prism divergence: 8°; prism convergence: 9°; "k": 1.09: "A": 0.79; and "P": 0.30. (Table 1)

Resection of the m. medial recti of the right eye for the length of 4 mm. was done on the 28th day after the 2nd operation.

Thirty days later (after the 3rd operation), the position of the eyeballs was nearly orthophoric at the gaze of a far away place and slightly deviated inward at the gaze of a near by place. (Fig. 3.) Prism divergence became 2.5°, prism convergence, 7°, "k" 1.18, "A" 0.92, and "P" 0.26. (Table 1)

Discussion

Why exophoria develops at the gaze of a far away place?

The patient has an extreme anisometropia of −10.0D in the right eye and−0.5D in the left eye. Further, the patient was 13 years old when the visual aquity of the right eye started to decrease to such an extent, that binocular vision was not possible any more. Previously Harada and I stated, that exotropia developed as a rule, when binocular vision was impaired after the age of 7 years. In this case this rule was followed and outward dsviation was considered to have resulted.

As etiological factors of the divergence excess, the following items have been suggested:

1. overactivity of the divergent center.
2. anomaly of the postural tonus of the muscular apparatus.
3. passive divergence due to elasticity of the orbital structures.

Overactivity of the divergent center alone, however, can not explain the fact of the divergent position developing at the gaze of a far away place when one eye is covered. It seems reasonable to consider the following mechanisms in order to explain the phenomenon: The outward deviation of the eyeball is caused by the relaxation of the m. medial recti due to weakening of the innervation of convergence in removal of fusion, and by the tonus of the m. lateral recti and elasticity of the orbital structures.

Why the degree of outward deviation decreases markedly in fusion-free position at the gaze of a near by place?

Attention is an important factor in maintaining fusion. Therefore, it is conceivable, that day-dreaming would cause an outward deviation as Knapp suggested. However, in this case, outward deviation did not occur during day dreaming at the

gaze of a near by point.

Although Swan stated that accommodation influenced significantly the gaze of a near by place, the right eye of this patient was of excessive myopia and accommodation did not occur at the gaze of a near by place. Accordingly, the influence of accommodation does not come into consideration.

According to my Haloscopic test, the accommodative convergence-accommodation ratio "A" in this patient was 0.66 which was not much different from the value in a normal adult, while the proximal convergence-accommodation ratio "P" was 0.35 which was remarkably larger than the normal value. As I reported previously, the "P" in most of the ordinary exophoric subjects is small and its average value is 0.03. In other words, proximal convergence in the ordinary exophoric is poor while it is excellent considerably in this case. At the gaze of a near by place, the excellent convergent action overcomes the exophoria and the degree of outward deviation decreases. This is the important difference between the ordinary exophoria and the divergence excess.

According to the common concept, the eyeball position at the gaze of near by place was taken as the standard, and the divergence excess was suspected, when the degree of outward deviation was high. However, I take the eyeball position at the gaze of a far away place as the standard and consider that exophoria disappears or diminishes at the gaze of a near by place by encellent convergent action.

Summary

A case of divergence excess was closely investigated, and the following hypothesis was presented.

1. Exophoria manifested at the gaze of a far away place in removal of fusion is caused by anomaly of the postural tonus of the muscular apparatus and by passive divergence due to the elasticity of the orbital structures.

2. The postion of the eyeball approaches to orthophoria at the gaze of a nearby place because the outward deviation described above is overcome by excellent proximal convergence under this condition.

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STUDY ON THE VISUAL FIXATION, ESPECIALLY ON THE PHYSIOLOGIC SCOTOMA PHENOMENON

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Introduction

When we ranke an effort to stress the visual fixation on the central area continuously without any ocular movement voluntarily added, a physiologic central blur of short duration will be sometimes found because of retinal fatigue. But after this moment appeared, if shifting of the ocular posture occurs in any way, this phenomenon will be suddenly disappearing with a newly focussed accommodation on the next fixating point. This physiologic phenomenon which has been already described by the author (1944), is very common in our daily life, while nowadays it remains only as a not yet further discussed problem in the ophthalmological area.

In the present paper, the author describes some experimental discussions on this conspicuous fact and its causative mechanism from an ophthalmological view point.

Experiments

Basic experiments on the phenomenon were carried out in 7200 times on 360 test groups by using some skilled normal persons to test with the author's method, which

Fig. 1. Test object.

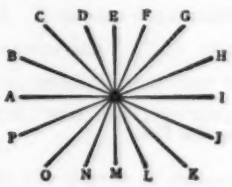
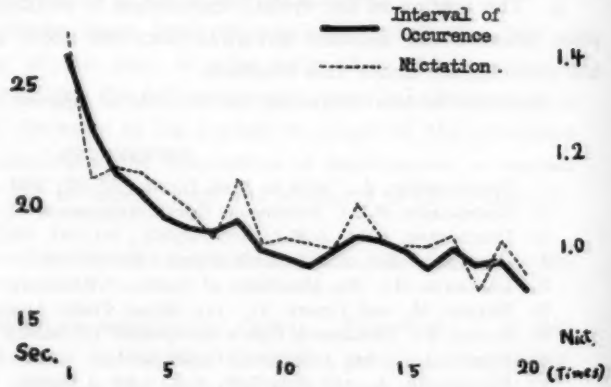


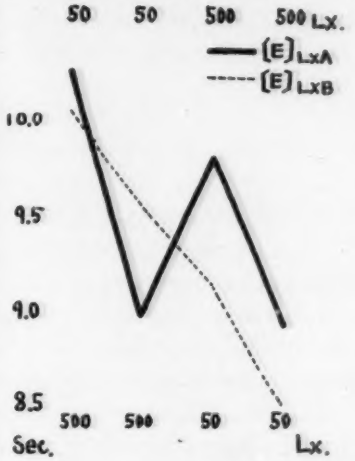
Fig. 2. Interval of occurence and nictation.



must be performed in a noiseless place in a room with two kinds of illumination, most in the night time, at random on the right or left eye, fixating on the test object with star-like 16 radiated black lines crossing at the central fixating point printed on white paper. (Fig. 1)

Each radiated line is composed of many dots which valued each 3 degrees as a visual angle. The fest is performed at two meter distance under illumination of two kinds, 50 and 500 Lux. When a sudden blur occurs on any part of the lines with monocular or binocular vision, the examiner marks the blurring area in the territory of the lines and the fixating time duration is estimated, furthermore, the number of nictation during this period is also observed at the same time. Thereafter, the lid must be closed for the next succeeding test.

Fig. 3. Illuminating condition & skill.



According of the results obtained with 15 normal persons in the test, the phenomenon occured with a duration of 3-14 seconds, showing, that a common phenomenon easily can be performed

Table 1. Visual Angle in Frequent Occurrence

Visual Angle	0°	3°	6°	9°	12°	15°
%	1509	— 24.7	2309	19.2	16.1	

Table 2. Occurrence & Terriory of Phenomenon

	Side / Cases	1	2	3	4	5	Total
R.	Left	72.2	51.1	98.0	69.4	59.7	68.6
	Center	3.1	3.4	0.2	7.2	1.5	3.9
	Right	24.9	45.5	1.8	23.4	38·8	27.5
	Upper	27.6	42.1	38.7	36.5	30.0	35.6
	Horiz.	2.8	6.1	0.5	14.5	4.4	7.1
	Lower	69.6	51.8	60.8	49.0	65.6	57.3
L.	Cases	6	7	8	8	10	Total
	Left	67.7	62.5	58.1	42.3	88.0	61.2
	Center	0.7	5.8	4.5	1.5	0.8	3.0
	Right	51.5	51.7	37.4	56.2	11.2	35.8
	Upper	50.9	60.3	63.2	47.2	7.9	47.0
	Horiz.	0.6	0.8	1·3	1.1	1.9	1.3
	Lower	48.5	38.9	35.5	51.7	91.2	51.7

under a definite condition by the author's method.

Occurence of the phenomenon is shown in Fig. 2. It may be considered that, occurrence seems to increase in the repeated test which is easily performed. Definite parallelism between the facility of occurence and the trend of the decreased nictation may be recognizable. As shown in Fig. 3, in regard to the illumination, a low illuminated condition will facilitate the occurrence of the phenomenon more than in high illumination. That is the clear step between 50 Lx and 500 Lx in Lxa. Furthermore, in the skilled person in this test, it is easier to recognize the phenomenon than in the non-skilled person.

In the majority of cases, occurrence in the paracental area as 3-6 degrees of visual angle should be most frequent. (Table 1)

Relation between Occnrrence and the Dominant Eye.

Occurrence of the phenomenon as to the area in the visual field on the test object was discussed by the auther as shown Table 2.

Directions the phenomenon appeared frequently are always-constants. Occurrence in which in left and lower half of the field is always frequent, especially, in the diagonal line the frequency was found to be as strong as 89% of occurrence, although there was no difference in the left or right eye of the use side. Furthermore, in the same tests with dextrocularity or sinistrocularity, definite interesting results are obtained. In the test with dextrocularity, therefore, a contraverse appearance is proved being almost of a different direction in comparison with that in sinistrocularity. Consequently, an increased occurrence in right and upper half of the field is evidently confirmed in the test with sinistrocularity.

From this fact, it may be reasonable to state, that the central suppression or conduction to occurrence of the phenomenon should be suggestive.

Influence of Nictation on Occurrence of the Phenomenon.

As above mentioned, the author presumed, that the phenomenon would be suppressed by ocular fixating movement or nictation. Because, when the phenomenon is interrupted, as the disappearance of the physiological blur in the test area, the minimum ocular movement and therewith accompanied nictation may occur in the tested eye observed by the author.

This fact would be suggesting, that the existence of the peripheral nervous influence, as the foveal movement of the fixation due to the physiological retinal fatigue, may be presumable.

According to individual cases of tested persons, the interval time of two nictations in the test duration was 175 seconds at the longest and 6.2 seconds at the shortest. So that a reasonable occurrence of the phenomenon is noted most frequently in the cases of skilled persons showing less nictation.

From these reasons, the author considers, that the ophthalmic entity of normal nictation is closely related to the occurence of the phenomenon and should be as follows:

1. Momentary laxity of the extrinsic muscles and Bell's phenomenon.
2. Protecting acceleration of the lacrimation to the ocular dryness.
3. Interruption of the light exposure on the retina.
4. Gentral laxity of the fusion, accommodation and convergence action. For the purpose to clarify the related nictation to the phenomenon, other new test objects with dotted radiation or oblique striped figures were used in the same observation of the author's phenomenon.

With these testobjects, the response of occurrence of the phenomenon by use of partial localized illumination or artificial lid setting was investigated. From these tests, in the localized illuminated field, occurrence is evidently suppressed like 89.4% of negative phenomenon obtained. The shifting of the covered area of the test field with an artificial lid set is most effective to prove a negative phenomenon, showing a decreased occurence like 93.9%.

These particular results should be remarkably revealing the fact, that the interrupted light exposure may decrease occurrence of the phenomenon, being under a similar condition to that in nictation during the appearance of the phenomenon.

Discussion

From the results obtained, the author's physiologic central scotoma phenomenon may be supposed to be due to the fixating retinal fatigue related to the foveal fixating movement, much more due to the form-vision and lesser due to the central nervous fatigue. Nictation, one of the part causation to the peripheral fatigue, will be likely to give a sufficient interpretation to the interruption of the phenomenon. Some interpretations to the fatigue, which have been stated by Bartley (1947) and Berens (1950) coincide almost with the author's consideration as to the phenomenon. Also, McFarland (1942) said, that normal nictation plays a role to prevent the retinal fatigue.

From the author's results like 2.8% of occurrence on the right side horizontal line or 3.8% of occurrence on the left side horizontal line in the test field, the meaning of Mariott's blind spot could not be presumable in relation to the entity of the phenomenon. From the fact confirming 69.4% of occurrence on the diagonal line, furthermore, Evans's retinal angioscotoma has also no relation with the phenomenon. Ishizu's maculo-coecal scotoma or Oshima's central field fatigue appears mainly in pathological eyes, being also in no relation to the author's phenomenon.

Summary

The physiologic central blur which occurs in the parafoveal fixating area, when a binocular or monocular central fixation is stressed continuously for a short time by the normal person, was discussed experimentally. This phenomenon presumed as a sign of retinal fatigue, should be mainly suppressed by normal nictation, by reason

of the interruption of the light exposure to the retina.

Some inconspicuous questions, however, like the central refractoric mechanism of the phenomenon or physiological and psychological response of the phenomenon, especially their relation connected with nictation, would remain to be clarified in further investigation. Therefore, the physiological paracentral shifting of the fixating ocular movement due to foveal fatigue should be a closely related problem on thə author's physiologic scotoma phenomenon..

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EXPERIMENTAL STUDIES ON THE ACTION POTENTIAL OF THE IRIS

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Part I. Stimulation of the Cervical Sympathetic Nerve

Detailed studies on pupillary movement have heretofore been done chiefly by the use of photography. In Japan, too, rather many investigations of this kind have been performed, and their results published. On the other hand, however, very few investigations have ever been carried out into the action potential of pupillary movement. Reid in 1895, and Braunstein in 1925 noted the action potential of the iris in experiments with cats and rabbits, but in 1927 this action potential of the iris was denied by Kogo in his careful check-up investigation. In 1946 Monnier, after throwing light into one human eye, recorded a slow potential variation in the other non-illuminated eye. In 1951 Dodt conducted experimental investigations into the c-wave of human ERG, and noted the effects of pupillary movement on the formation of the c-wave. He further placed electrodes directly on the exposed iris of the cat, and recoded the action current released by dilatation of the pupil due to stimulation of the cervical sympathetic nerve. In 1954 Kawabata, with use of cats, indirectly induced the action potential of m. sphincter pupillae which accompanied the consensual reflex of the

pupil. This, Kawabata's investigation was a check-up study of Monnier's, but it was more carefully conducted than the latter.

The so-called electropupillograms have so far been obtained by means of indirect induction. In recent years Dodt is the only investigator who, using cats, has tried the method of direct induction, but slow potential variations recorded by him are not much different from those obtained by indirect induction. On this account the present author, doubting the validity of Dodt's experimental results, carried out a check-up investigation (Part I); and further recorded pupillary movements due to stimulation of the oculomotor nerve (Part II); and finally experimentally re-examined the so-called electropupillography (Part III). The results obtained are given below.

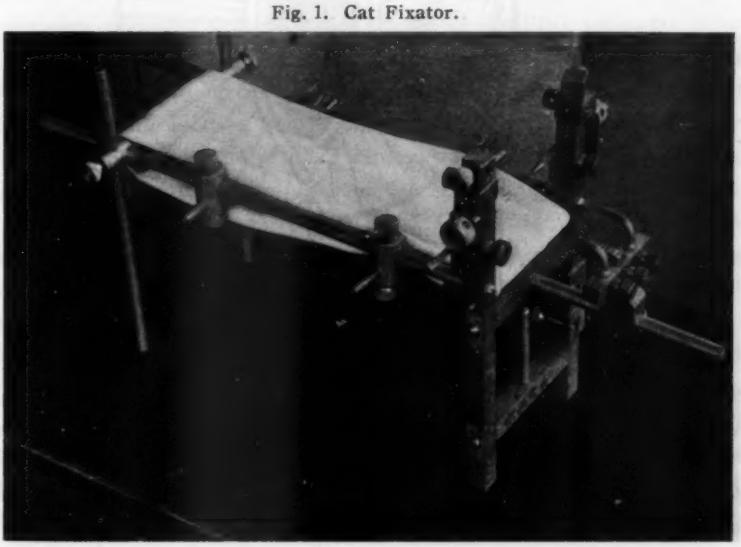
Methods

Experimental Animals. Cats weighing 2-3 kg. were used. (1) Operative Procedures. The intraperitoneal injection of Isomytal in 50 mg. per kg. body weight quantities was used for anesthetization. The cervical sympathetic nerve trunks on both sides were completely separated from the parallel-running vagus nerves. The nictitating membrane was removed from the experimental eye, and all the external muscles were severed. In the case of direct induction the cornea was removed.

(2) Fixation. A special instrument for fixation was manufactured by removing a micromanipulator from a Johnson-type stereotaxic instrument. (Fig. 1)

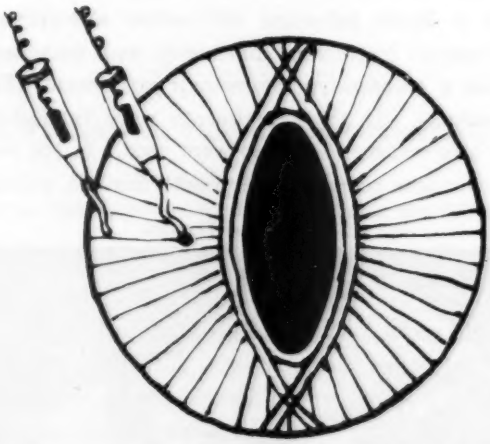
Experimental Apparatus. All the experiments were conducted in a sealed room. (1) Electrode. Zinc-zinc sulfate electrodes were used. In the case of direct induction from the iris the cornea was removed after Dodt's method, and different and indifferent

Fig. 1. Cat Fixator.



electrodes were placed along the direction of m. dilatator pupillae. (Fig. 2) The site of the latter electrode was thermocoagulated, and a unipolar induction was conducted. The cotton thread at the tip of the electrode was made as thin as possible to be placed on the iris. In the case of indirect induction the eyeball was not opened, and the different electrode was put on the limbus, while the indifferent one was inserted deep into the subonjunctival tissue from the wound formed by the severance of m. rectus superior, and placed on the sclera near the equatorial region. (2) The stimulating electrode (silver wire 1 mm. in diameter) was placed between the superior and the inferior cervical ganglion. In the early stage of experiments the inductorium was used for stimulation, and not only coil distance, but also resistance in the primary circuit was varied. Later the universal electronic stimulator was used to give a frequent rectangular-wave stimulation. (3) Amplifier and Recorder. Sanei Company's amplifier for the measurement of bioelectricity was used. This amplifier has a switchover device for three time constants. The time constant mostly used was 6 seconds. For recording either a penoscillograph or a Brown-tube oscillograph was used.

Fig. 2. The pupil of the feline eye (Raselli).



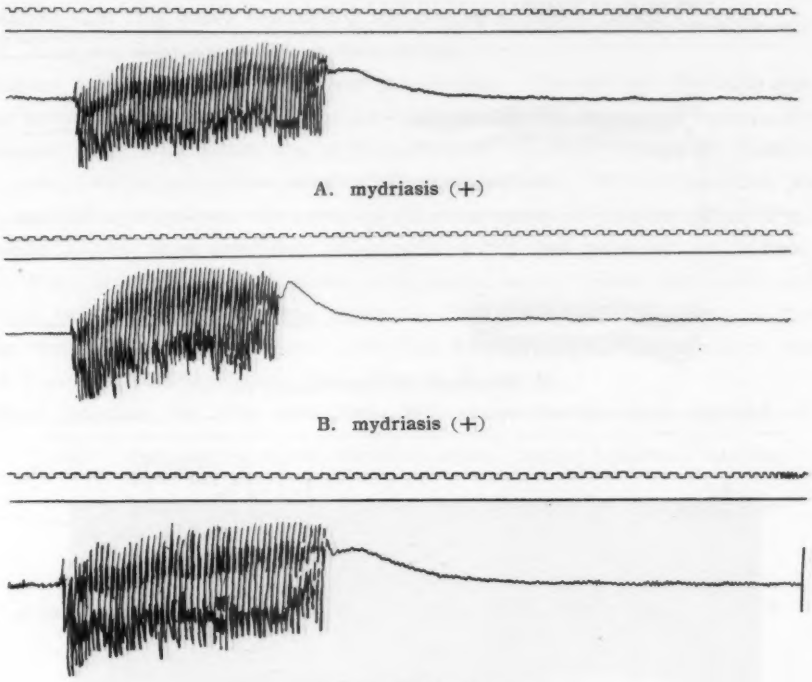
Induction unipolarized by placing the indifferent electrode on the thermocoagulated site. Zinc-zinc sulfate electrodes used. (After Dodt's method)

Results

1) Stimulation with the Inductorium

As Arlt, Schiff and Hamdi had reported, a single stimulation was incapable of causing mydriasis, and so a frequent stimulation was necessary. The induction electrodes were placed as shown in Fig. 2. When 2 volts were used as the primary voltage of the inductorium, and coil distance was made 10 cm. long, the stimulation continued

Fig. 3. Stimulation with induction current. Coil distance 10 cm.



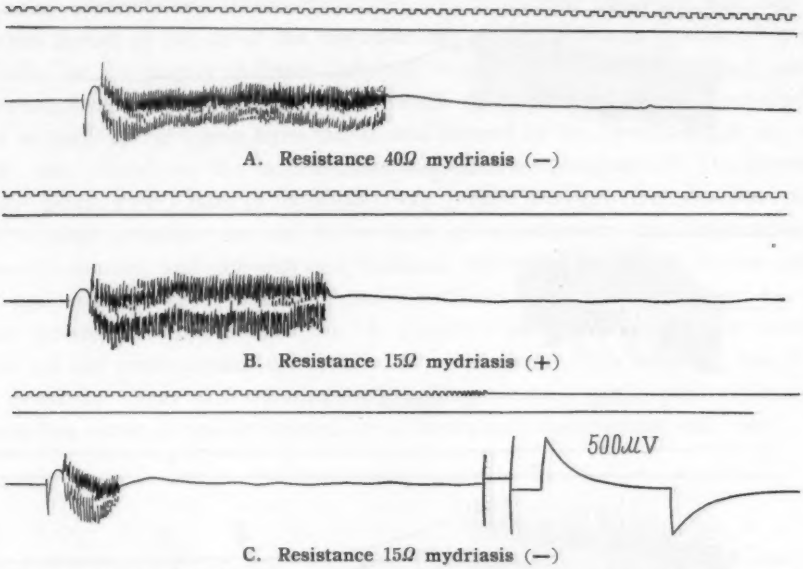
A. mydriasis (+)

B. mydriasis (+)

C. mydriasis (+)

for 1-1.5 second produced definite dilatation of the pupil. In this case, as shown in Fig. 3, a potential variation similar to the c-wave of the ERG appeared following the artifact due to stimulation. In order to ascertain whether this potential variation had been caused by the action current of the iris, it was attempted to determine the thereshold value of stimulation which would elicit pupillary movement. For this purpose resistance placed in the primary circuit was varied, while coil distance was fixed at zero, and stimulation time at about 1-2 seconds. Mydriasis was found first to occur, when the resistance was reduced to 15 Ω (Fig. 4, B and 5, A). No marked potential variation was observed. When a resistance of 40 Ω was placed in the primary circuit, stimulation continued for 2.7 seconds did not produce any pupillary movement, and such was also the case with stimulation continued for 0.65 seconds with a resistance of 15 Ω. But it was noted, that even in these cases, regardless of no movement of the pupil, a potential variation made its appearance (Fig. 4, A and C). Because of this finding, the nature of this potential variation which bore resemblance to the c-wave became problematical. To institute a control experiment, both of the electrodes were removed from the iris, and short-circuited in the saline solution, while the cervical sympathetic nerve was stimulated as formerly (Fig. 5,

Fig. 4. Stimulation with induction current. Coil distance 0. Resistance placed in the primary circuit.

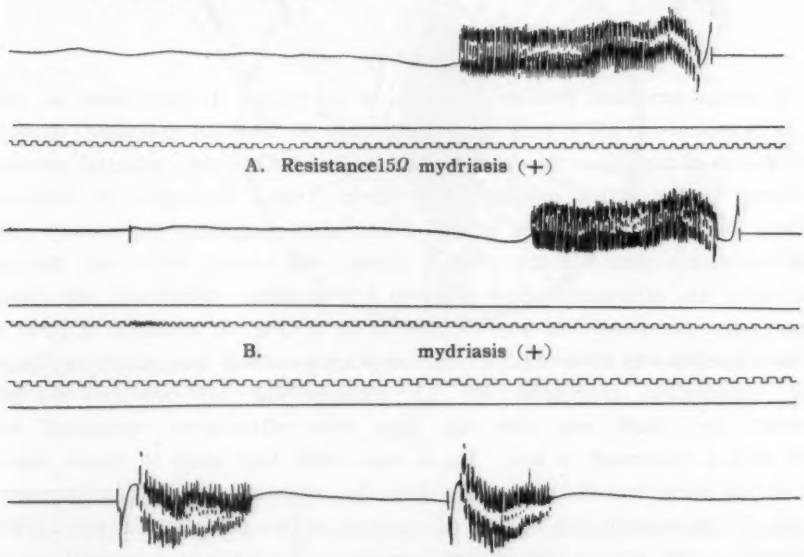


A. Resistance 40Ω mydriasis (—)

B. Resistance 15Ω mydriasis (+)

C. Resistance 15Ω mydriasis (—)

Fig. 5. Stimulation with induction current. Coil distance 0; resistance placed in the primary circuit 16Ω.



A. Resistance15Ω mydriasis (+)

B. mydriasis (+)

C. mydriasis (—)

B and C obtained from control experiments. The induction electrodes removed from the iris. and short-circuited in the saline solution. A obtained by placing electrodes on the iris.

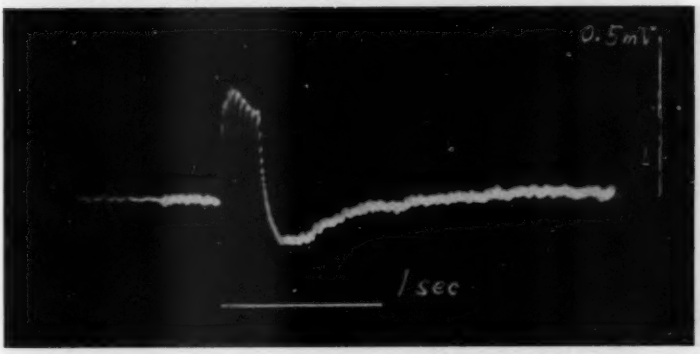
B and C). When Fig. 5, A is compared with B and C, it wil be known that it is hasty to conclude that this curve resembling the c-wave is due to action current.

2) Frequent Rectangular-Wave Stimulation

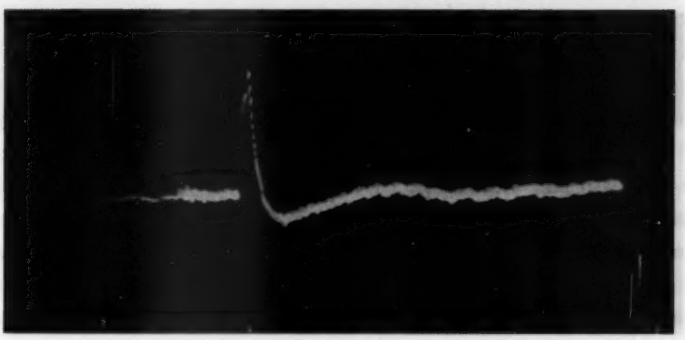
Indirect Induction. The eyeball was not opened. The different electrode was placed on the cornea, and the indifferent one on the sclera in the equatorial region. Frequent rectangular-wave stimulation was given under the following conditions: pulse width 2 msec.; pulse frequency 20 cycles ; generating voltsage 2 volts. When stimulation was thus given, marked mydriasis was observed. A potential variation was also noted (Fig. 6, A). Mydriasis became more prominent when pulse width was increased to 5 msec (Fig. 6, C). When the induction electrodes were short-circuited under the above conditions, a similar potential variation was observed (Fig. 6, B and D). That is, the same finding was obtained even where there was to be no action potential; tne curves in A and C are not distinguishable from those in B and D.

Direct Induction. In this case, too, the same results were obtained as when

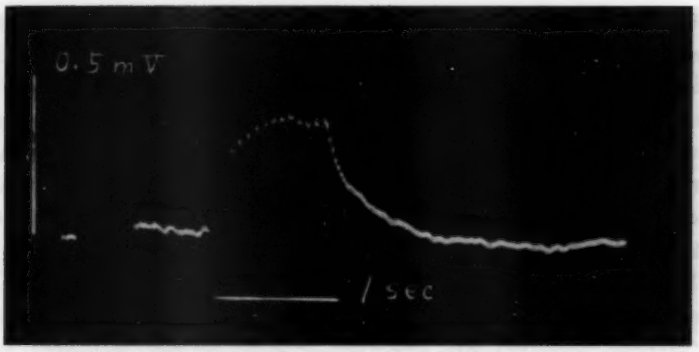
Fig. 6. Frequent rectangular-wave stimulation. Indirect induction (induction electrodes placed on the cornea).



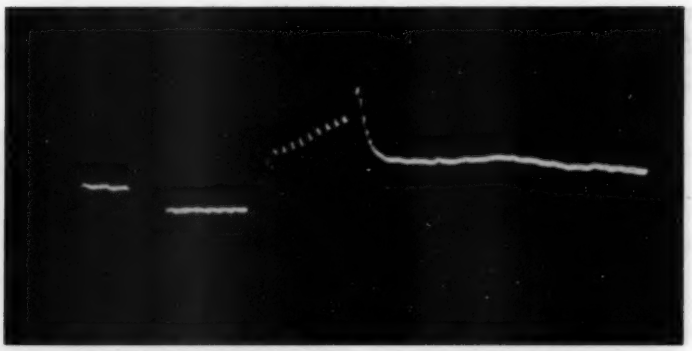
A. 2 msec.; 20 cycles; 2 volts. mydriasis (+)



B. 2 msec.; 20 cycles; 2 volts. mydriasis (+)
Induction electrodes short-circuited on the cornea.



C. 5 msec.; 20 cycles; 2 volts. mydriasis (+)



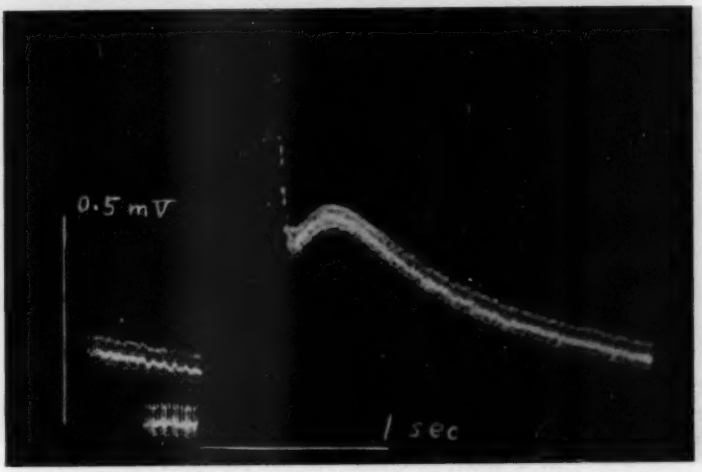
D. 5 msec.; 20 cycles; 2 volts. mydriasis (+)
Induction electrodes short-circuited on the cornea.

the inductorium had been used. Very mild mydriasis was observed when frequent stimulation (2 msec., 50 cycles, 1.5 volt) was given, and also was noted a potential variation seemingly due to action potential. (Fig. 7, A and B) This time again, however, when the electrodes were short-circuited on the iris, a nearly similar curve to the above was obtained. (Fig. 8)

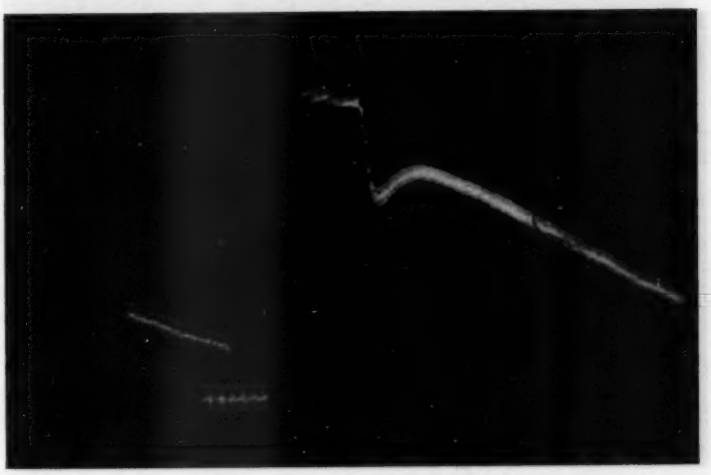
Discussion

In 1895 Reid placed induction electrodes directly on m. sphincter and dilatator pupillae of the cat, and noted that the stimulation of the cervical sympathetic nerve produced negative or positive changes in the string galvanometer. Brücke and Orbeli, however, conducting the same experiments in 1910, denied Reid's experimental results. Kogo also stated in 19 27 that it was impossible to exclude current variations caused by the movement of the sites in contact with electrodes. In 1925 Branustein made studies of the action potential of the iris with use of cats, and reported that the stimulation of the cervical sympathetic nerve elicited an action current from the iris

Fig. 7. Frequent rectangular-wave stimulation. Direct induction (induction electrodes placed on the iris).



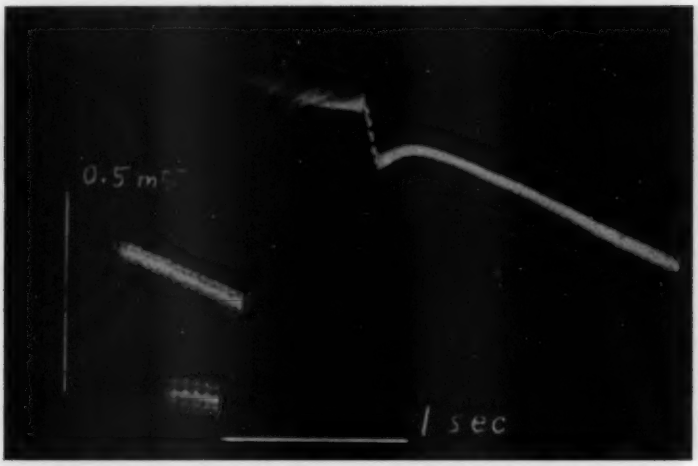
A. 2 msec.; 50 cycles; 1.5 volt. mydriasis (+)



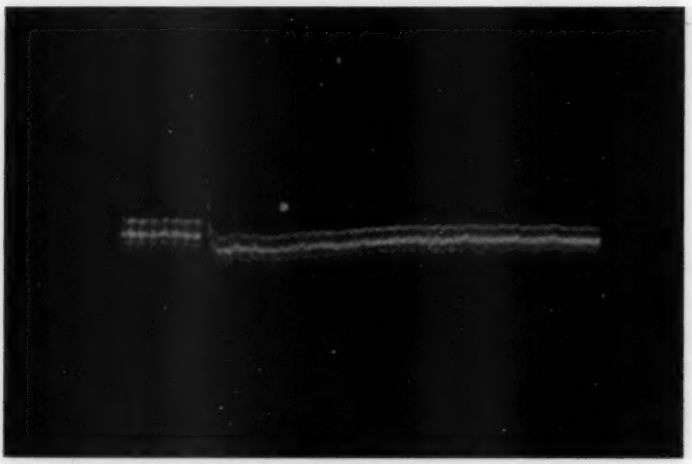
B. 2 msec.; 50 cycles; 1.5 volt. mydriasis (+)

of the same side through direct and indirect induction. In 1927, however, Kogo conducted a close check-up investigation, and stated that no true action current of the iris was demonstrable by Braunstein's method. That is, when 2 volts were used, and the coil distance of the inductorium was made 15 cm. long, the stimulation of the cervical sympathetic nerve caused mydriasis, and simultaneously produced an electric variation, it is true, but even when there was no mydriasis, coils being 30 cm. apart, a similar electric variation was observed. Such being the case, Kogo held it impossible

Fig. 8. Frequent rectangular-wave stimulation.



A. 2 msec.; 50 cycles; 1.5 volt. mydriasis (+)
Induction electrodes short-circuited on the iris.



B. Single stimulation (2 msec. 1.5 volt)

to attribute this electric variation to the action current released by the movement of the iris.

In 1951 Dodt tried to induce the action current of the iris by placing electrodes directly on the iris of the cat. Concerning the direct induction of the action current of the iris there are no other recent papers except Dodt's report of this experiment. Dodt removed the cornea, placed two electrodes on m. dilatator pupillae, and by stimulating the cervical sympathetic nerve, obtained the curve which is given in Fig. 9, B. He made the coil distance of the inductorium 15 cm. long, and used d'Arson-

Fig. 9. B. The cervical sympathetic nerve of the cat stimulated with induction current (coil distance 15 cm.), and action current obtained from the iris by direct unipolar induction.
C. An ERG of the human eye (Dodt).

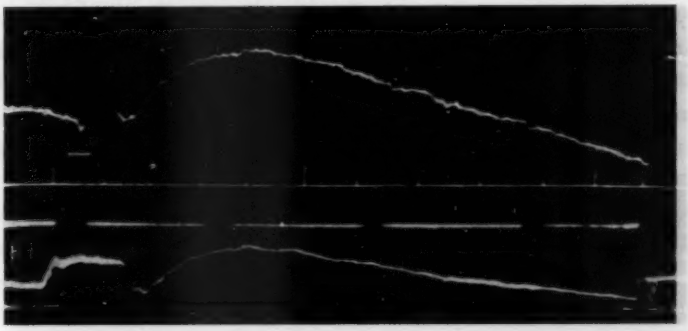


Table 1.

Cases	Frequent Rectangular-wave Stimulation		Amplitude
	Conditions	Duration (sec.)	(mV)
Fig. 7A	2 Msec; 50 Cycles: 1.5 Volt	0.4	0.5
Fig. 7B	DO.	0.53	0.5
Control Fig. 8	DO.	0.83	0.6

Table 2.

Cases	Stimulation with Inductorium		Amplitude
	Conditions	Duration (sec.)	(mV)
Fig. 3A.	C.D. 10 cm	2.1	0.5
Fig. 3C.	DO.	2.1	0.4
Fig. 4B.	C.D.0 Resistance 15 Ω	2.2	0.08
Fig. 5A.	DO.	2.2	0.2
Control Fig. 5B	DO.	1.8	0.2
Control Fig. 5C	DO.	0.8	0.1

val's electrades which were, as shown in Fig. 2, brought into contact with m. dilatator by cotton threads. According to him, the potential obtained was 0.2 mV., and a longer stimulation produced a greater potential variation and vice versa. But in the present check-up investigation, the results of which, being measured, are given in Table 1, the same potential variation was obtained regardless of the length of stimulation time, and moreover even in control experiments. The results of stimulation with the inductorium, as recorded by the penoscillograph, are given in Table 2. In control experiments the induction electrodes were removed from the experimental animal, and short-circuited in the saline solution, but nonetheless the same finding was obtained.

This fact throws a doubt on Dodt's so-called action current directly induced from the iris of the cat. The curve recorded in Fig. 9 B bears a definite resemblance to those in Figs. 7,3,4 B and 5A, and further even to those in Figs. 8 and 5 B and C obtained from control experiments. The delated potential variation following the artifact, which is observable in all these figures, and which looks like the c-wave is perhaps nothing but an oscillation of the ground-line; this oscillation occurs as a reaction to the great force entering the amplifier. When a single stimulation was applied, only the artifact due to stimulation was observed, and there was no oscillation of the ground-line, to say nothing of pupillary movement.

The foregoing results were obtained with zinc-zinc sulfate electrodes. Though the electrodes were in contact with the iris through cotton thread, it was impossible to exclude the movement artifact. This difficulty of exclusion may be especially greater with silver electrodes. As a frequent stimulation must be applied to get an effective response, an oscillation of the ground-line is inevitable.

Bülbring and Hooton (1955) measured the membrane potential of m. sphincter of the rabbit iris preparation, using microelectrodes, but they, too, admitted the unsuitableness of the iris preparation for the study of activity changes because of the impossibility of excluding movement artifacts. Viewed in this way, the failure of the present attemt to record the action current directly from the iris in situ was only natural.

As to indirect induction, the present author, like Kogo, could observe nothing but an oscillation of the ground-line due to frequent stimulation just as in the case of direct induction.

Conclusions

1. With the use of cats it was attempted to induce action current from the iris at the time of pupillary movement due to electric stimulation of the cervical sympathetic nerve, but this attempt has failed with either indirect or direct induction.

2. Direct induction was conducted after Dodt's method, and from the results obtained it was inferred, that his so-called action current of the iris had been nothing but an artifact.

Part II. Stimulation of the Oculomotor Nerve

In the case of stimulation of the cervical sympathetic nerve the action current of the iris, which was to be induced, was covered up by large artifacts due to repeated stimulation. The present author, therefore, turned his eye to the oculomotor nerve as a site to which a single stimulation might prove effective.

Methods

Experimental Animals. Cats were used. The intraperitoneal injection of Isomytal was used for anesthetization. A large part of the skull ranging from the

parietal to the temoral side was excised, and the oculomotor nerve was sought at the base of the brain. When the ciliary nerve ganglion and the short ciliary nerve were looked for, the lateral and upper walls of the orbit were removed. After due operative procedures the animal was fixed with the fixator (Fig. 1.).

Experimental Apparatus. The stimulating electrodes (Ag) were completely insulated. Two such electrodes were combined and bent like a hook so as to be used in a narrow space. As to the induction electrode, stimulating apparatus, amplifier and recorder, refer to Part I. Indirect induction was used throughout.

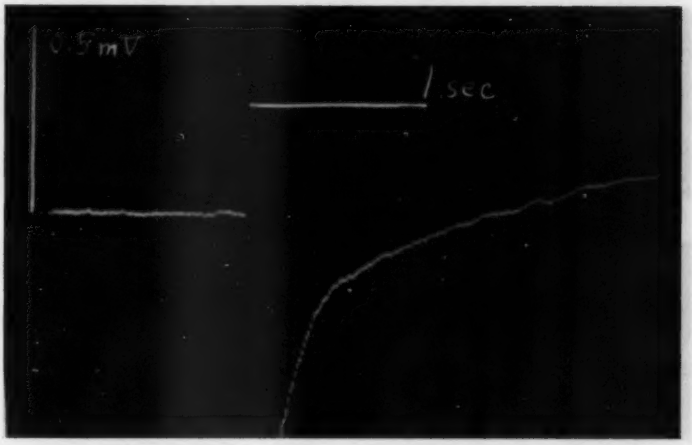


Fig. 10. A. Stimulation of the short ciliary nerve with a single rectangular-wave current. (2 msec.; 8V.) mydriasis (±)

B. Control experiment. Two electrodes short-circuited on the cornea. mydriasis (±)

Results

First of all, it had to be ascertained, whether a single stimulation was really effective or not, but the relation between stimulation and response proved rather much more complicated than had been first imagined. Only a few cases responded to a single stimulation, and even these cases showed such large artifacts, that it was extremely difficult to distinguish an electric variation due to the action current. High voltage, long stimulation time, and the proximity of the site of stimulation to that of induction all contributed to make the difficulty greater. Moreover, as the time constant used was as long as 6 seconds, such large sartifacts as shown inF ig. 10 were unavoidably produced. When a single rectangular-wave stimulation was reduced in time and strength to 2 volts/2 msec., pupillary reation was no longer observable. Experiments with repeated stimulation were not conducted as it was assumed, that the electric variation would probably be covered up by large artifacts as in the case of experiments of Part I.

Discussion and Conclusions

Lngendorff (1894), Reid (1895), Kuntz and Richins (1946), Nishida and Koike (1954), Armaly (1959) and many others reported on the relationship between pupillary reaction and stimulation of the oculomotor nerve. The present author, too, has recognized the complicated nature of this relationship, and noted that a single stimation could succeed in evoking response only in rare cases. As weak stimulation is ineffective, the production of artifacts is inevitable. Accordingly it is concluded that the stimulation of the oculomotor nerve, like that of the cervical sympathetic nerve, is unsuitable for the study of activity changes.

Part III. Consensual Light Stimulation

As it had been ascertained, that the stimulation of the cervical sympathetic nerve or the oculomotor nerve was unsuitable for the induction of the action potential of the iris, light was chosen as a means of stimulation.

Methods

Experimental Animals. Cats were used. Either the intramuscular injection of curare in 5 mg. per kg. body weight quantities or the intraperitoneal injection of Isomytal was used for anesthetization. Light reflex was maintained for about 30 minutes under such anesthesia. The fixator shown in Fig. 1 was used for fixing the animal. The nictitating membrane was removed from the experimental eye, and all the external muscles were severed. Human cases underwent only instillation anesthesia.

Experimental Apparatus. (1) Electrode. Zinc-zinc sulfate electrodes and a black-stained Nagata-type contact-lens (Fig. 11) were used. Canthotomy was performed,

Fig. 11.

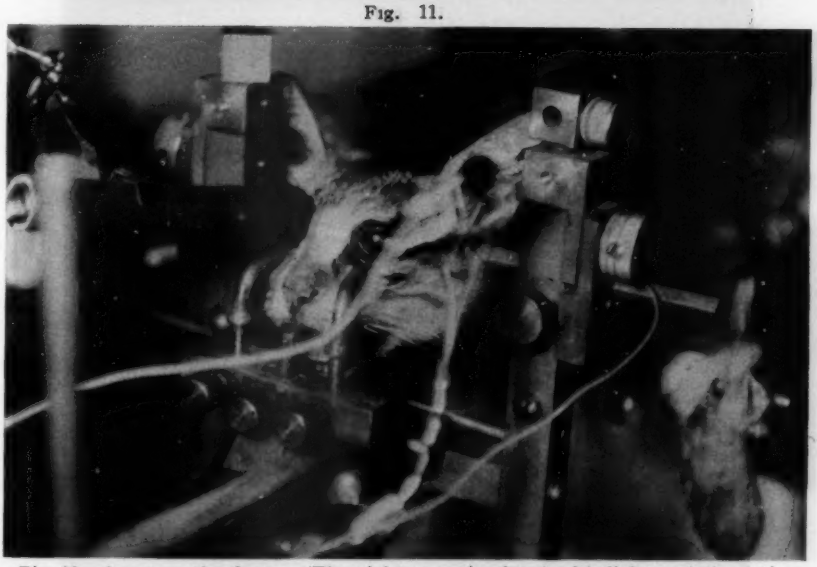


Fig. 12. A cat on the fixator. (The right eye stimulated with light, and the action current induced from the left eye.)

and the indifferent electrode was subcutaneously fixed at the wound thereby formed. In human cases it was placed on the skin between the eyes. The different electrode was brought in contact with a spongel inserted into the hole of the contact-lens. (2) Stimulating Apparatus. A 3.8-volt bulb was put into a metal cylinder, and lighted with a 6-volt storage battery. This cylinder was covored with tube-shaped black paper. A black-cloth tube was attached to this paper tube, and applied to the eye. The contact-lens being placed on the experimental eye, the leakage

Fig. 13. EPGs of feline eyes.

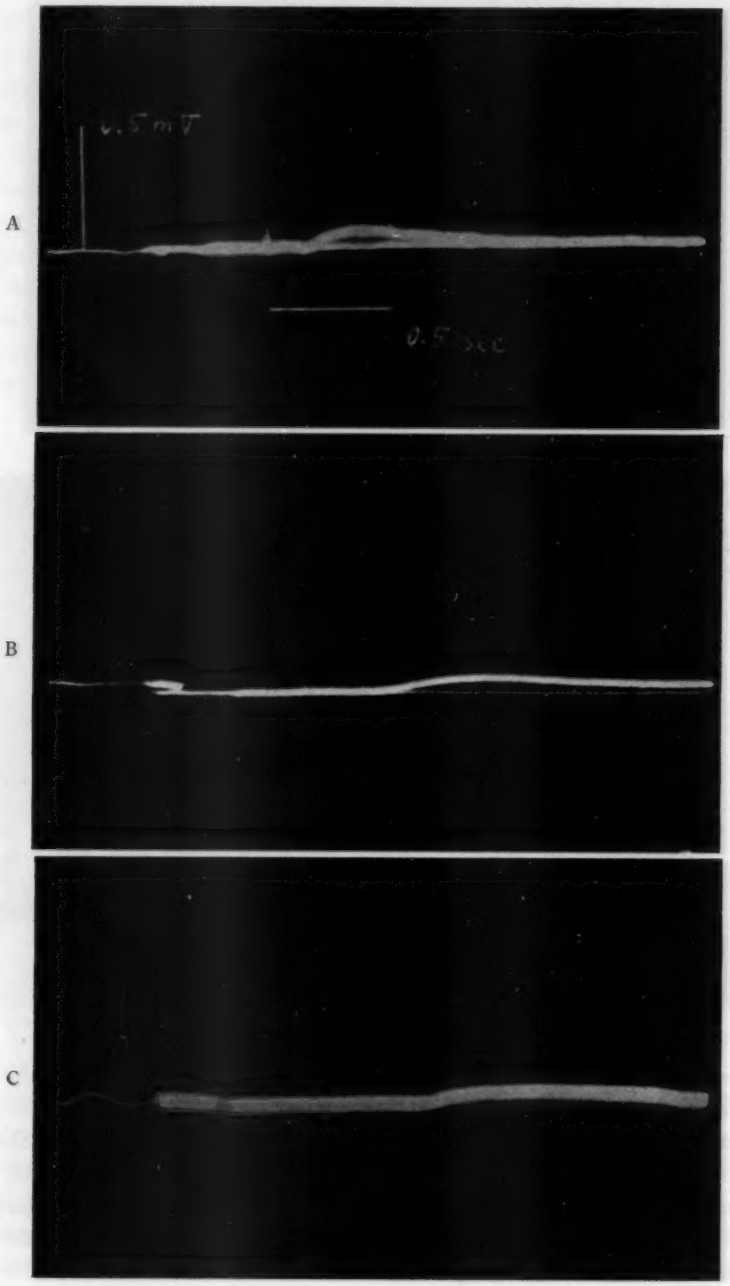
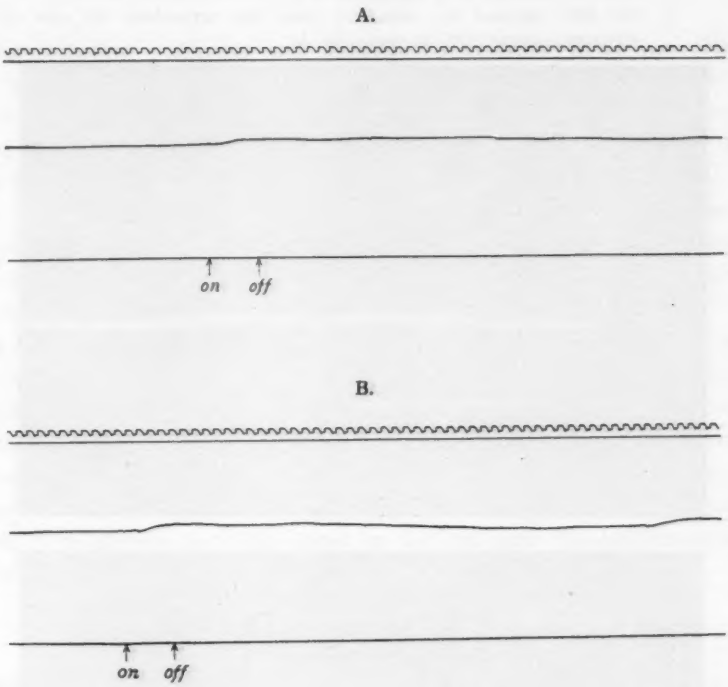


Fig. 14. EPGs and an ERG of human eyes.



C. ERG of the individual whose EPG isshown in B.

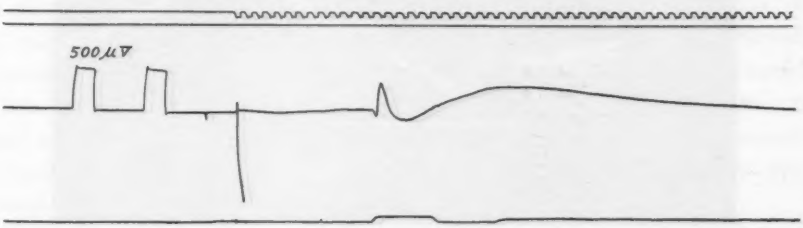
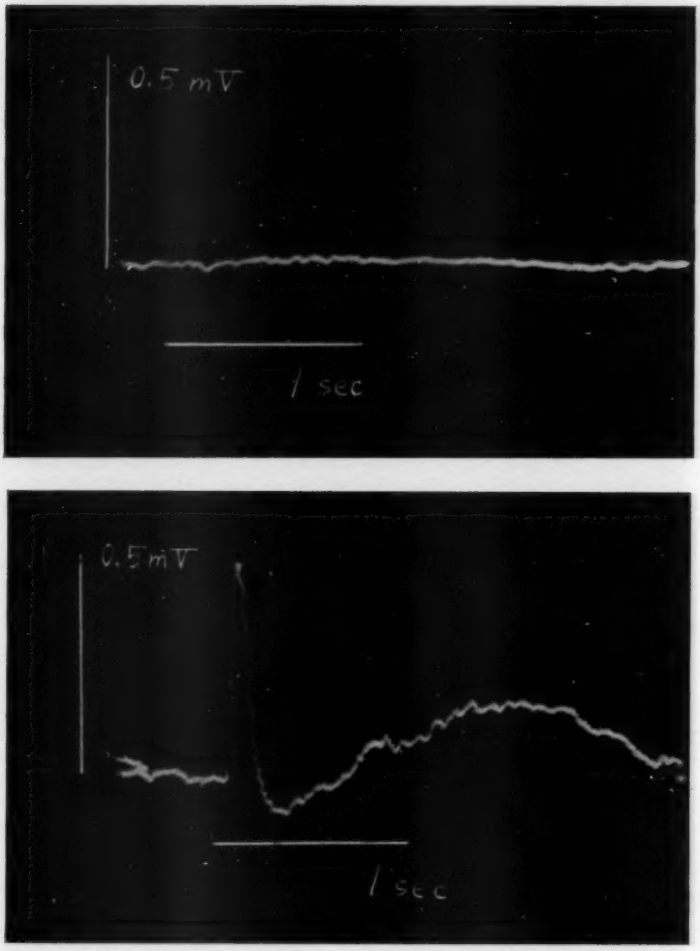


Table 3.

Cases	Latent time (sec.)	Culmination time (sec.)	Duration (sec.)	Amplitude (mV.)
Human Fig. 14A.	0.15	0.45	Unmeasurable	0.06
Fig. 14B.	0.23	0.59	2.25	0.07
Feline Fig. 13A.	0.22	0.37	1.09	0.08

Fig. 15. A. Induction electrodes placed on the iris of the left eye after removal of the cornea. The right eye stimulated with light. (The indifferent electrode inserted into the subcutis of the canthotomy wound.)
B. The ERG obtained by induction from the cornealess left eye of the individual whose EPG is shown in A.



of stimulating light was doubly prevented. The intensity of illumination was maintained at 920 lux throughout, and the stimulation time was adjusted by anelectron-tube timer to 1.0–1.5 second. When a Brown tube was used for recording, spikes of electro-magnetic induction at turning on and off were substituted for light signals, and so recording of spikes sometimes failed. When a penoscillograph was used, a part of light was received into a photoelectric tube for amplification, but in this case, too, recording of signals very frequently failed owing to the weakness

of light. (3) As to the amplifier and recorder, refer to Part I.

Results

Indirect Induction. Monnier and Kawabata's so-called EPGs are obtainable by indirect induction from the corneal surface of the action current of the iris elicited by consensual light reflex (Fig. 13). EPGs of healthy human adults are shown in Fig. 14, A and B. In C is given an ERG of the individual whose EPG is shown in B for the sake of contrast. Amplitude, latent time and other data, being measured, are given in Table 3. It will be known from Figs. 13, 14 and Table 3 that the curvature of EPG bears resemblance to that of the c-wave of the ERG. The EPG of the human eye do not essentially differ from those of the feline eye in amplitude, curvature and time relationship.

Direct Induction. Strong contraction of the iris and rigiditas pupillae result from the fall of intra-ocular tension occurring after the removal of the cornea, and as a matter of course the consensual light reflex disappears. The attempt to induce an action current from such an iris naturally failed, as shown in Fig. 15, A, and Dodt's so-called consensual retinal c-wave was not observed. But a typical ERG was obtained from the same eye of the same case without changing the sites of electrodes, as shown in Fig. 15, B. (The different electrode placed on the iris, and the indifferent one inserted into the subcutaneous tissue of the wound formed by canthotomy.)

Discussion and Conclusions

In 1946 Monnier, using human subjects, obtained a response similar to the c-wave of the ERG from the pupillary reflex, and coined the word 'Electropupillography' (EPG). In 1951 Dodt noted an extra-retinal, pupillary c-wave in human ERG, and stated that this wave could be induced consensually. In Japan Kawabata, with the use of cats, succeeded in recording the action potential of m. sphincter elicited by the consensual pupillary reflex. The present author, too, has successfully obtained EPGs from cats and human subjects by means of consensual light stimulation. But the attempt to induce an action-current directly from the iris by consensual light stimulation has miscarried; this attempt has been ascertained to be practically impossible.

Final Summary

1. Dodt reported on the direct induction of the action current of the iris by stimulation of the cervical sympathetic nerve. In Dodt's case this action current appeared as a slow potential variation similar to the c-wave of the ERG. The present author checked up Dodt's investigation, and demonstrated that this potential variation was nothing but an artifiact.

2. Induction by stimulation of the oculomotor nerve ended in failure owing to the appearance of large artifacts.

3. Light stimulation is best suited for the study of the action potential of the iris. By this means the present author could record the so-called EPG. But direct induction is practically impossible with this method.

4. The perfect exclusion of movement artifacts is indispensable for the success in induction, but the extreme difficulty of inserting electrodes into the micorscpic muscles of the iris makes the experiment of induction in situ practically impossible. Placing of the electrodes on the iris surface leaves much roon for the appearance of movement artifacts. Of course artiacts due to stimulation also disturb potential recording. Stimulation artifacts, however, will be excluded in future by the development of a perfect isolator and a dual beam oscilloscope.

In short, the so-called EPG could be obtained through indirect induction, but the direct induction of action current from the iris in situ failed. This failure seems unavoidable at the present level of technical development.

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TREATMENT OF MYOPIA WITH LOCAL USE OF NEOSYNEPHRINE HYDROCHLORIDE

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Introduction

Medical therapy of so-called pseudomyopia was first attempted by Wells and Donders by means of Atropine in the early days of the last century. Thereafter various agents such as Pilocarpine, Calpinol, Ephedrine, alkaline solution, Vagostigmine, Buscopan, Rot-pon and Banthine for local use, and Vagostigmine, Imidalin, Myanol, Calcium, Vitamine B_1 and Atraxin for systemic use have been tried. All of these should not be regarded as satisfactory agents in respect of continuity of the effect and ill sicle effects even though some insufficient results are obtained. On the other hand, the incidence of myopia in Japan shows gradual increase again after the Second World War, therefore establishment of the method of its treatment or prevention must be a matter of primary concern.

Various agents possibly effective on myopia were tried by the author on some several hundred subjects among the outpatients of the clinic since 1955, for the sake of finding some clues to the problem. From the therapeutic results gained in approximate 450 patients, Neosynephrine hydrochloride (N.S.) seems to be most effective of all the agents employed.

Subjects

The subjects for the present trial are limited to the patients complaining of visual disturbance who suffer from refractive error or accommodative anomaly with other wise no ophthalmological findings. As prolonged treatment and prolonged observation are needed, all the patients asking for relieving myopia are employed as subjects without any consideration of the factors: degree and duration of myopia, age of the patients, wearing or not wearing spectacles, fundus changes and heredity.

Examination and Therapeutic Procedure

At the first examination, naked eye vision, corrected vision, accommodating power, phoria, curvature of anterior surface of the cornea are examined. Especially it was endeavored to find out pseudomyopia by means of the fogging method using convex lenses.

For determining vision, Ishihara's International Test Type was used under the illumination of 150 lux. Examination of vision was held only once in two weeks or once a month in order to exclude the subjects to get accustomed to the Test Type.

Nearpoint of accommodation was measured by means of Ishihara's Accommodometer five times, of which the mean value was employed. From that value accommo-

dating power was calculated in terms of dioptre. Those who have asthenia accommodationis or large fluctuation of the near point were excluded.

The refractive state having been determined, the subjects were told to instill 5% solution of N.-S. himself, 3 times at several minutes interval every night before going to bed. Generally 2 week treatment was employed as a therapeutic course and one more course was added, when improvement was observed.

Though some subjects complained of slight irritating on instillation, they recovered to normal at the next morning. Other ill side effects such as focusing difficulty were never observed.

Determinations of the results were made at the end of the therapeutic course of 2 weeks and later 16 to 18 weeks after that.

As a matter of convenience, standardization of the results was made as follows.

Complete: naked eye vision 1.0 or better and no myopia detected with retinoscopy.

Remarkable: naked eye vision improved 4 columns or more on the Test Type, or decrease of degree of myopia 1 dioptre or more.

Favorable: naked eye vision improved 2 columns or more, or a decrease of 0.5 dioptre or more.

Unchanged: naked eye vision inproved less than 2 columns or a decrease of refraction less than 0.5 dioptre.

Deteriorated: naked eye vision deteriorated or degree of myopia in-creased relative to those of the first examination.

Astigmatism, combined if any, the refractive degree of the maximal meridian was employed without any consideration of the axis.

Results

Of 85 subjects (170 eyes) treated with N.S., 47 subjects (94 eyes) were followed up over 3 months, whose age distributes between 7 and 21 (Details should be refered to another paper, by the author, Acta O. Jap. vol. 63, No. 14,1959).

Table 1 shows the summary of the results. Approximately 90% of the subjects at the end of the course and approximately 70% at the last examination (further 16 to 18 weeks later) was improved respectively. Moreover it is remarkable, that the subjects considered to be of "complete" cure were found in approximately 16% and 9.5% respectively at each time.

Table 1.

	End.	After 5 M. latter
comp.	16	9
rema.	28	15
favo.	36	38
uncha.	11	23
det.	0	4

Figure 1 and 2 shows the comparison of the condition before and after the therapeutic course as to naked eye vision and the refractive state respectively. The figures suggest that, with a few exceptions, the subjects that nere cured "completely" had previously nak-

Fig. 1.

Bef. \ Aft.	0.15	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.5	Total
0.15		2		1	1								4
0.2		3	1	2	2	1	3						12
0.3			3	3	5	4	2		1	1			19
0.4		1		1	3	4	3	2	2				16
0.5				1		1	2	1					5
0.6								1		3			4
0.7							3	4		1	2		10
0.8								2	4	5	2		13
0.9										2	6		8
1.0											1		1
1.2											2		2
1.5													0
Total	0	6	4	8	11	10	13	10	7	12	13	0	94

Fig. 2.

Bef. \ Aft.	-3.5	-3.25	-3.0	-2.75	-2.5	-2.25	-2.0	-1.75	-1.5	-1.25	-1.0	-0.75	-0.5	-0.25	0	Total
-3.5				1												1
-3.25				1												1
-3.0			2	1			1									4
-2.75				1	2											3
-2.5								1								1
-2.25							1	1	1							3
-2.0							1	3	4	2	1					11
-1.75									4	2	1		2			9
-1.5							1	2		3	5		1			12
-1.25										1	1	1	1	1		5
-1.0											1	6	2	3		12
-0.75											1	3	6	7	4	21
-0.5													1	3	5	9
-0.25																0
0															2	2
Total	0	0	2	4	2	0	4	7	9	8	10	10	13	14	11	94

ed eye vision of 0.7 or more, or a refractive error of 0.75 dioptre or less. This will be an information of further study of the medical therapy of myopia.

Figure 3 shows the course of the therapeutic results of N.-S. of all the cases represented by the mean value of accommodating power, naked eye vision and refractive degree. It will be noticed, that both naked eye vision and refraction have been improved considerably though a slight reversion is seen, and even 5 months after the first examination, increase of the former by 0.23 and decrease of the latter by 0.41 dioptre in average are shown. This fact suggests, that the efficacy of N.S. is of considerable continuity. While, the accommodating power shows a slight gradual decrease.

When the subjects are devided into 2 age groups (15 or younger and over 15), the therapeutic effect in the older group shows to be more or less similar to that in the younger, which had better results than previously expected. This would be possibly due to the fact, that nearly all of the group have a slight degree of myopia.

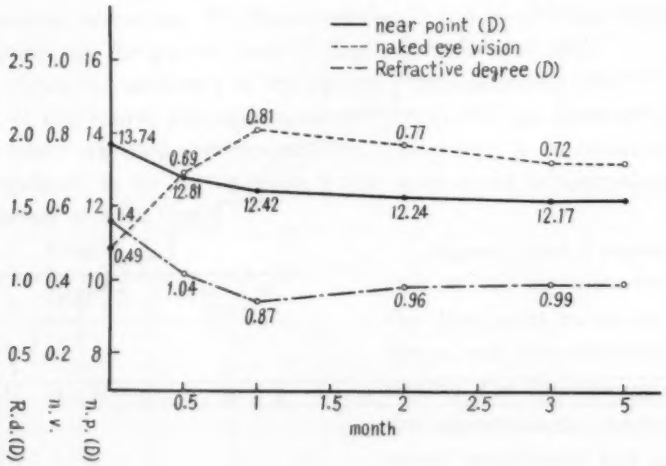
The interval between onset of the treatment and that of myopia dose not seem to have much influence on the results, but in the early stage of myopia, a little better result was obtained.

Although there were not any definite difference in the therapeutic results between the subjects with and without fundus changes, in the latter a slightly better result was shown when compared.

Discussion

Since first decribed in American pharmacopoeia in 1934, Neosynephrine hydrochloride, one of the new synthetized sympathomimetics, has been widely used. It is said to be most excellent among the relative amines because of: extremely slight

Fig. 3.



toxicity, good stability, and strong vasconstrictive and vasopressive action. Since the agent was introduced to Japan several years ago, it has been widely applied in the area of general surgery and now it is about to take the place of Adrenaline of Ephedrine as Hypertensive agents pre and under operation. Also in the area of ophthalmology, it rapidly has come to general use as a mydriatic because of its various advantages: rapid beginning of and short duration of mydriasis, no ill effect on ocular tension and or central retinal artery pressure, relatively slight effect on accommodation etc.

The agent, analogous to Adrenaline and Ephedrine, of which the chemical structure is l-α hydroxymethyl-amino-3-hydroxy-ethylbenzene-hydrochloride, has a rapid mydriatic action because of relaxing the pupilloconstrictor and of stimulating the pupillodilatator, but its paralizing action on the ciliary muscle is slight, and its vasconstrictive action is regarded to be 1/5 relative to adrenaline.

Yamaji's experimental study, using a 5% solution of the agent, shows, that pupillodilatating, beginning in 5 to 20 minutes, reaches its maximum in 30 to 60 minutes and reversed to the previous condition in 2 to 7 hours, while its accommodating power reaches its minimum in 30 to 60 minutes, when it reduces by 1.5 to 3.0 dioptre.

Employing various concertrations of N.S., Miyazaki and others concluded, that the more concentrated the solution the more accommodation paralysis occurred, for example, with 10% solution, considerable, and with 2% solution around 2 dioptres. Similar experiments made by the author on emmetropes and on myopes likewise showed the decrease of the accommodation by 1.5 to 2.0 dioptres.

The cycloplegic action of N.S., though weak as described above, becomes considerably effective by prolonged use, and moreover, also considerable continuity can be expected. Cycloplegic action of N.S. compared with that of Atropine is shown in Figure 4. It will be found, that N.S. is much superior to Atropine in continuity of the effect, though vice versa in rapidity.

Prof. Yuge had recommended local use of Pilocarpine before going to bed as a treatment of pseudomyopia. A small number of the subjects similarly treated by the author with Pilocarpine shows some what inferior results, than with N.S., though the difference is not so definite. (Figure 4).

In the present series of the experimental therapy of myopia, various agents, were used. The summary results are shown in Figure 5. It can be said, that N.S. is the most effective agent in respect of an increase of naked eye vision, decreasing of refraction and continuity of the effect.

The working mechanism of the agent is not yet completely solved. It is possibly due to cycloplegic action (or relaxation of abnormal ciliary tension) and to some probable factors such as ocular ischemia.

At any rate, it is unreasonable to discuss about the treatment of myopia neglecting congenital disposition, and in the present stage, we can not help but saying

Fig. 4.

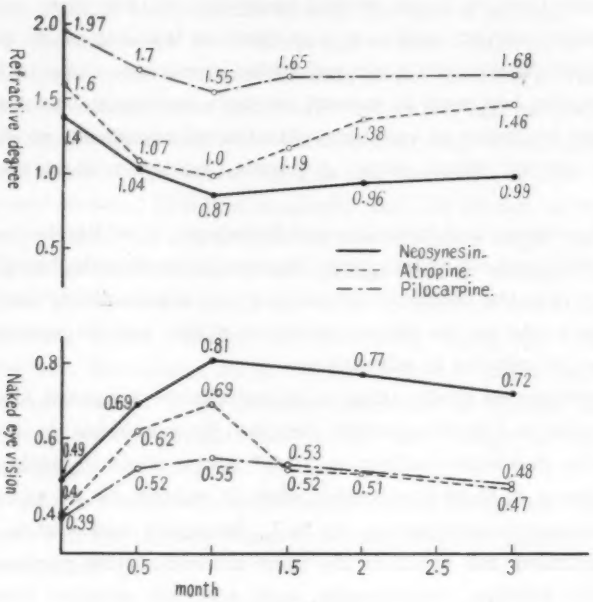
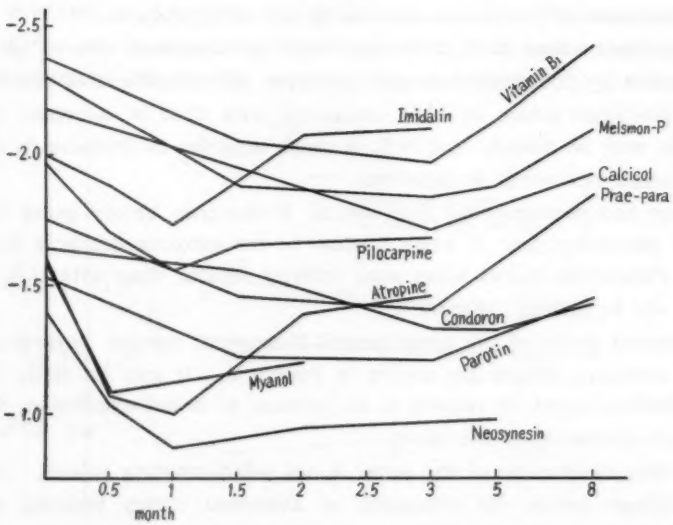


Fig. 5.



impossible to relieve the condition simply by medical therapy. Since physical dispositiion and environment are concerned in the development of myopia, it is essential that the prevention and the therapy of the condition should be elaborated

on persistently for a long time. Besides, as the figure suggests, the efficacy of any treatment should not be determined too soon.

The author is not positive about what kind of hystological changes occur by the prolonged use of N.S., According to Prof. Otsuka's animal experiment, held before, the refractive state tended rather to wards myopia with that prolonged use of Atropine and Ephedrine. Therefore, further study is necessary to clarify that respect.

Conclusion

Local application of 5% solution of Neosynephrine hydrochloride at home before sleeping is a very simple method of treatment of myopia and yields no ill side effects.

The results was most satisfactory, that even 4 to 5 months after the completion of the treatment, increase of naked eye vision by 0.23 and a decrease of the refractive degree by 0.14 dioptre in average respectively could be attained when compared to those of at the first examination.

This method should be recommended for the treatment or prevention of the progress of myopia.

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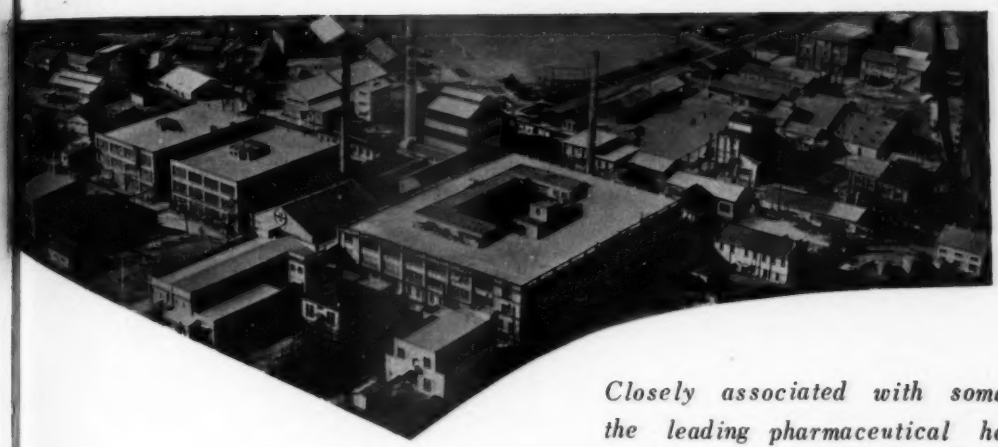

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